Vol. 14 OCTOBER, 1943 No. 4

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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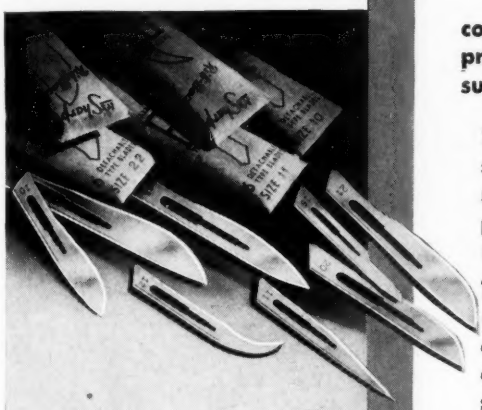

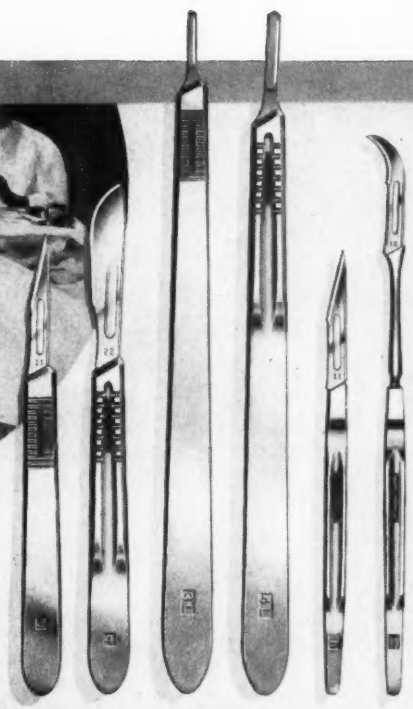

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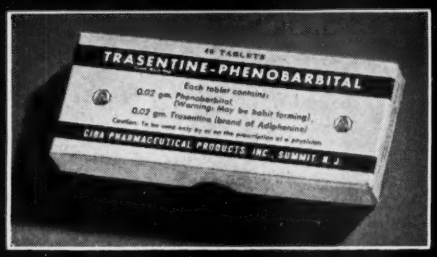
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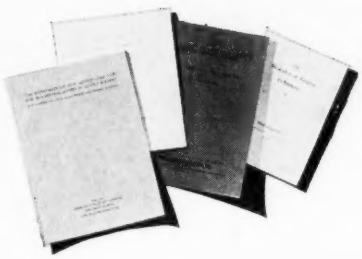

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*Harvey, Samuel C.: Annals of Surgery 102:946 (Nov.) 1935.

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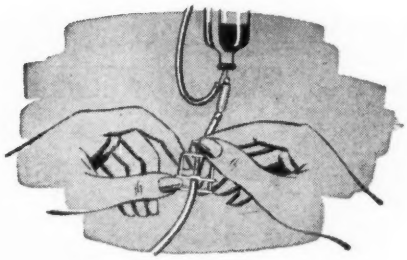

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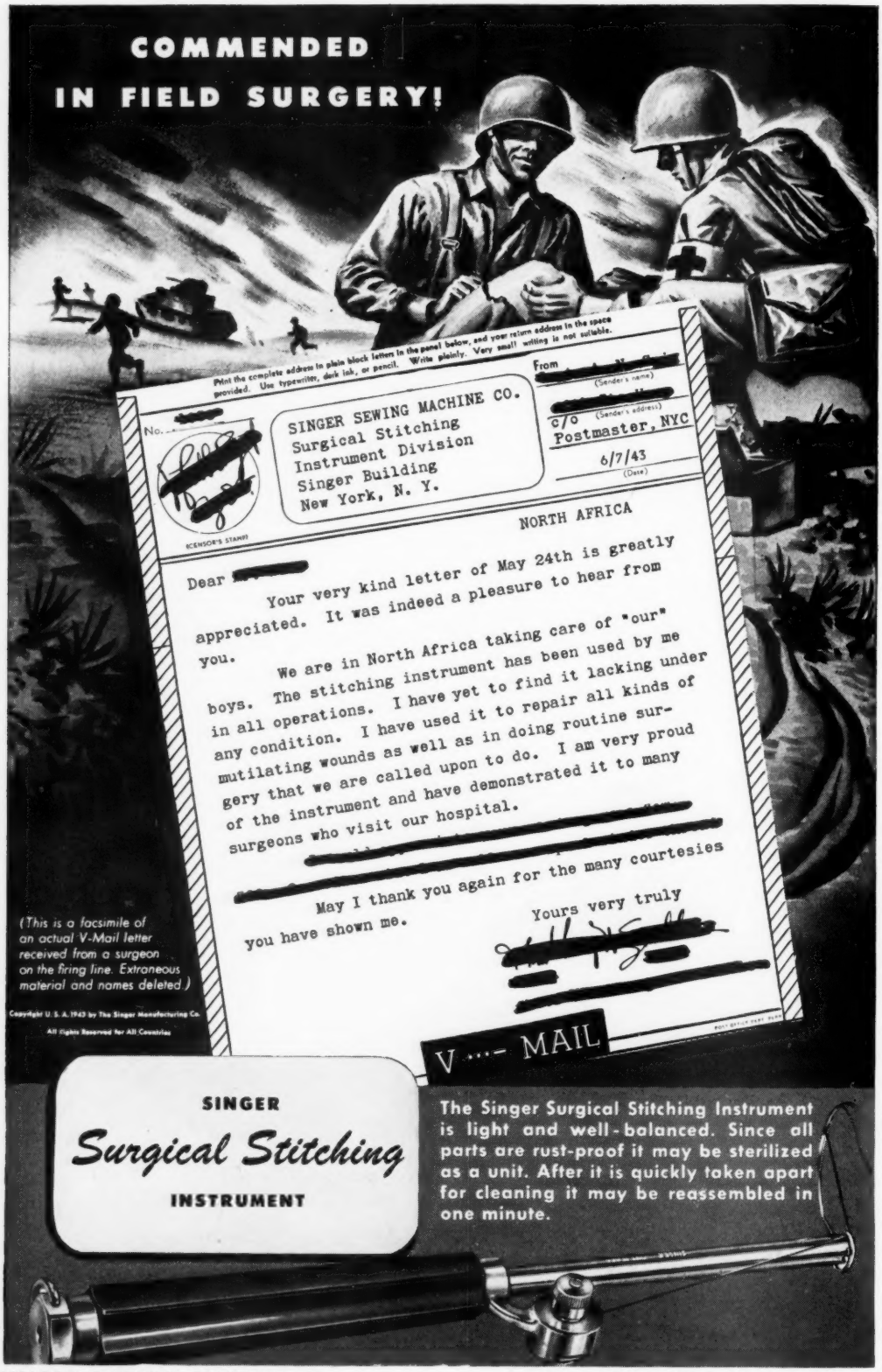
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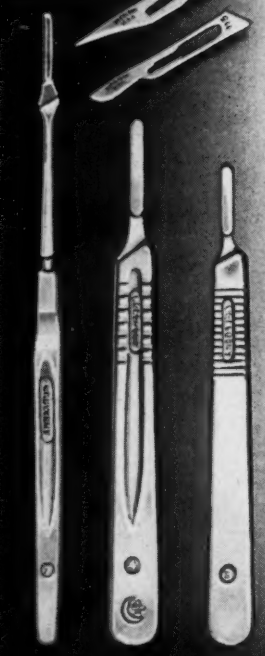

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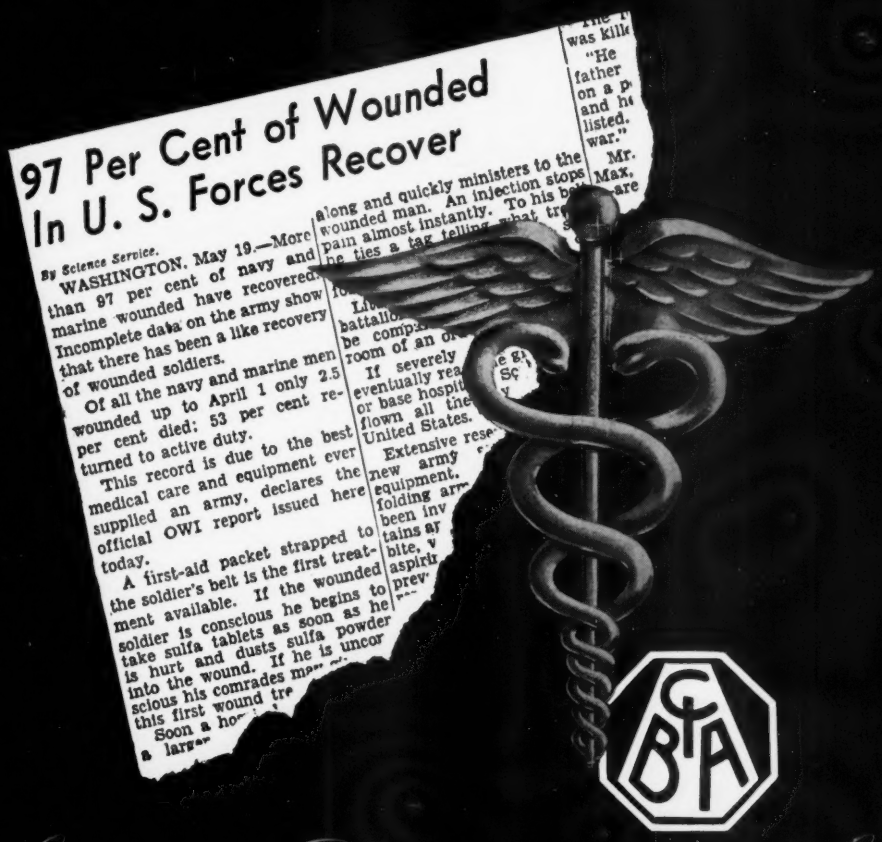
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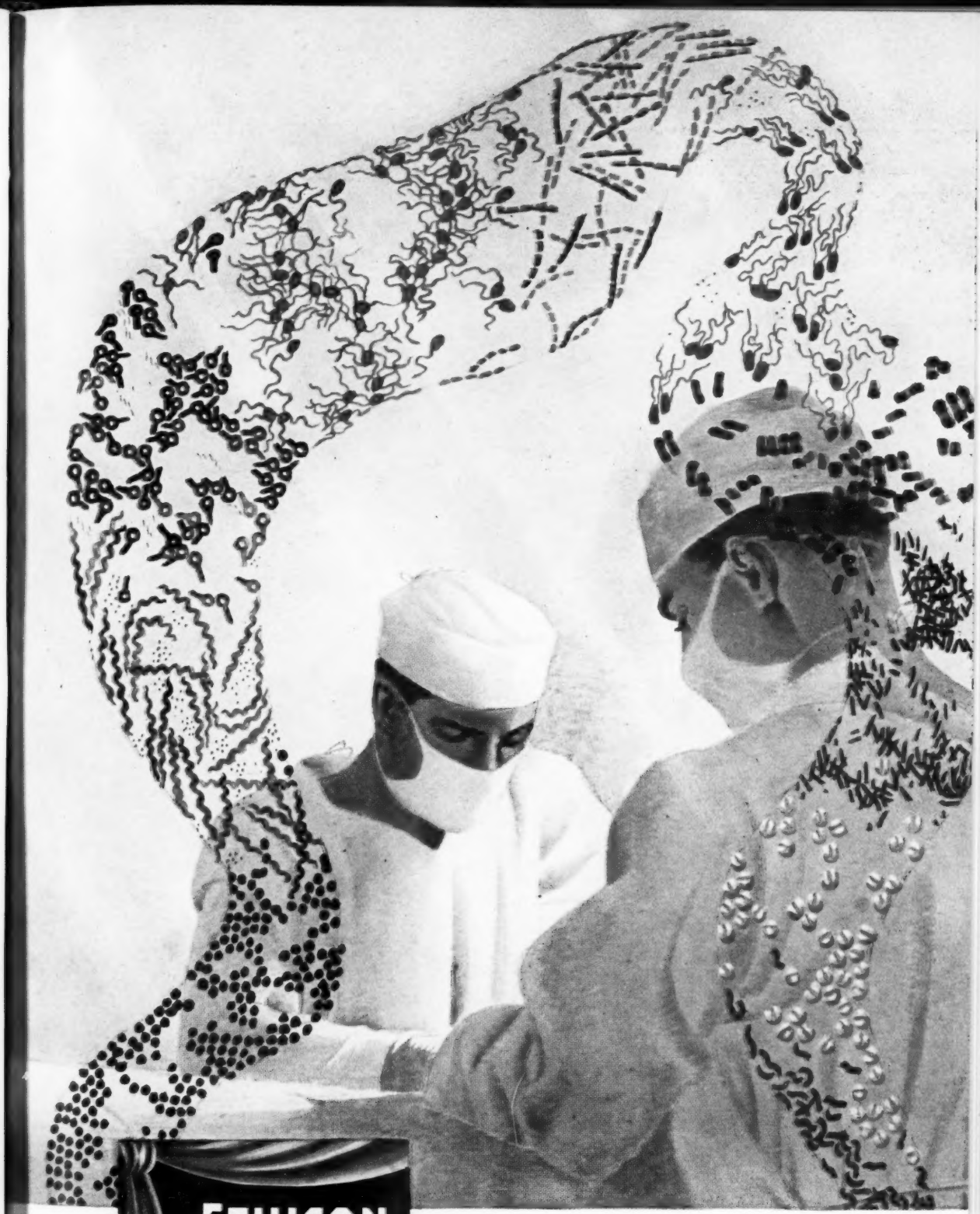

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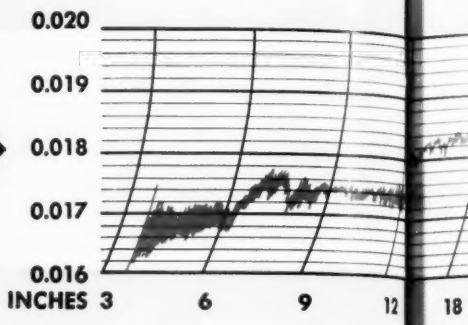

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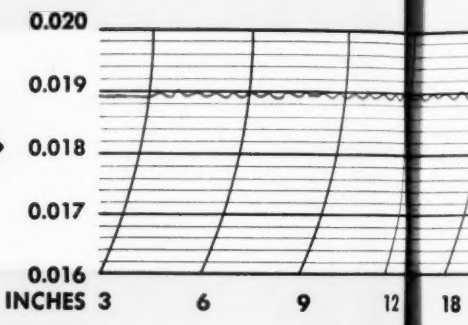

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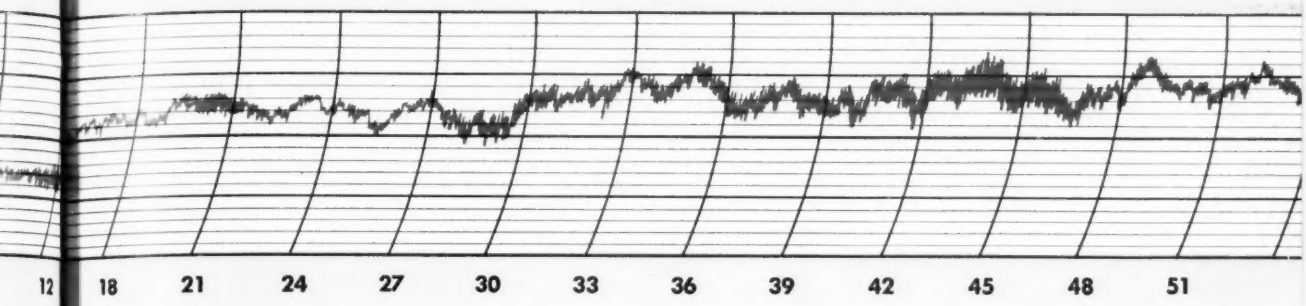

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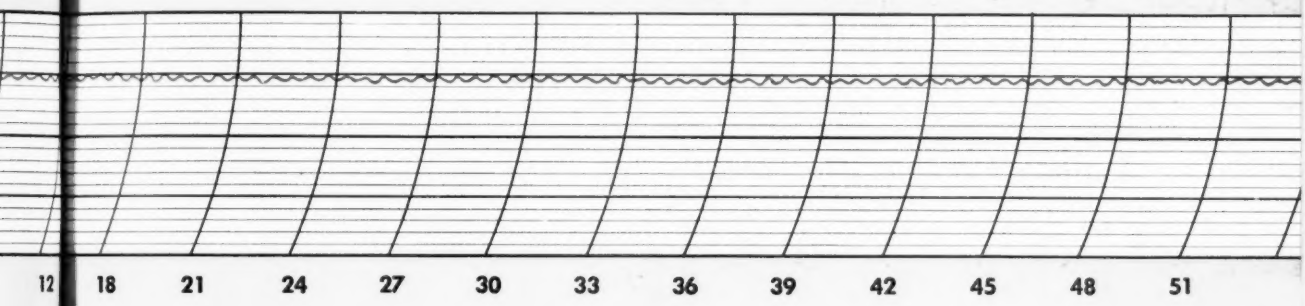

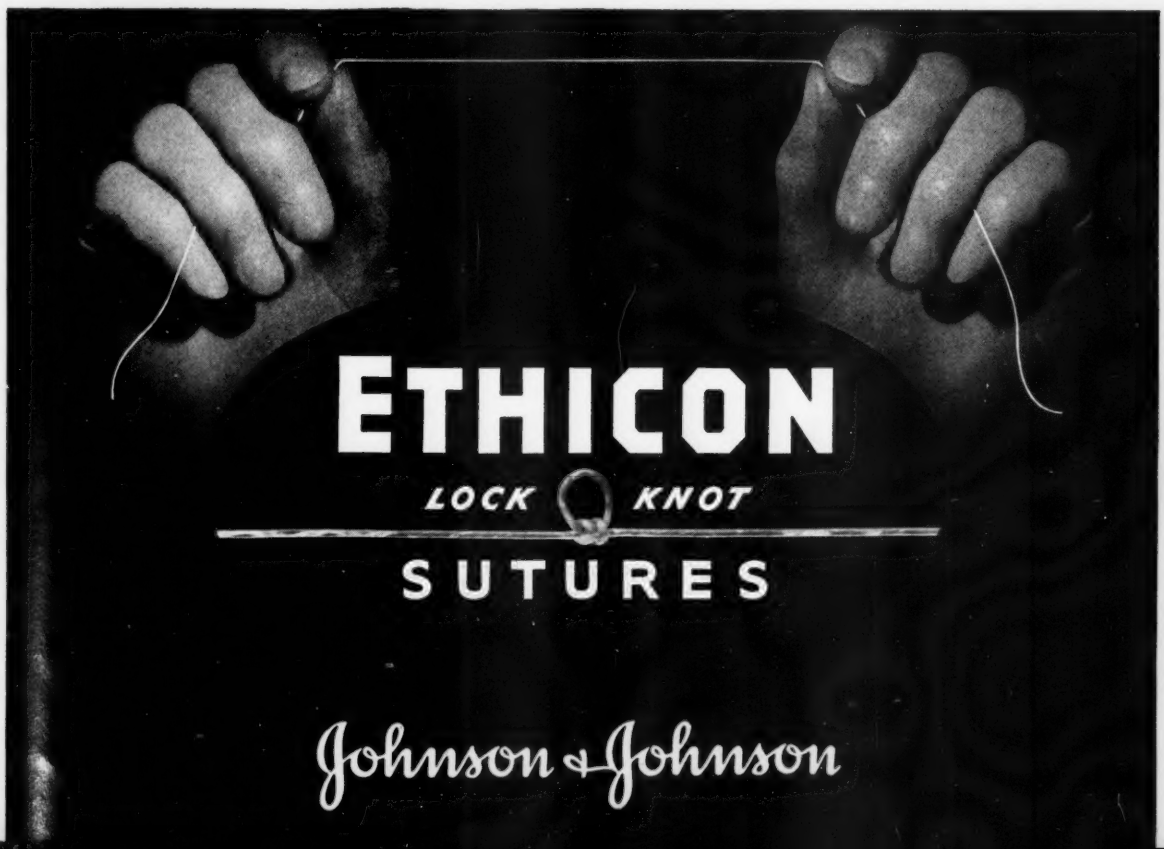

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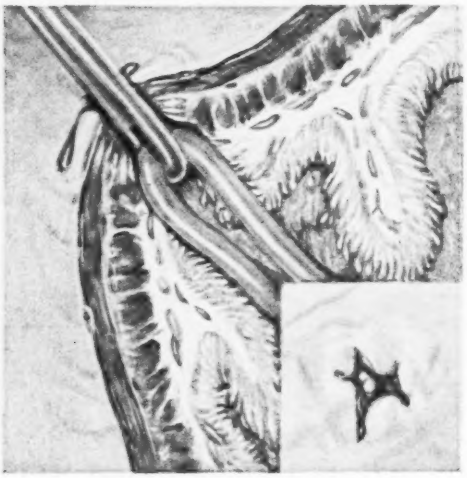

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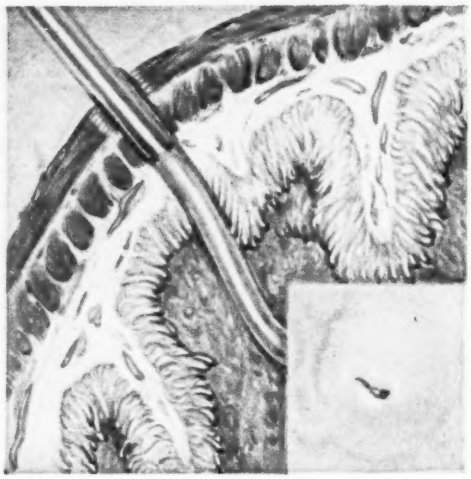

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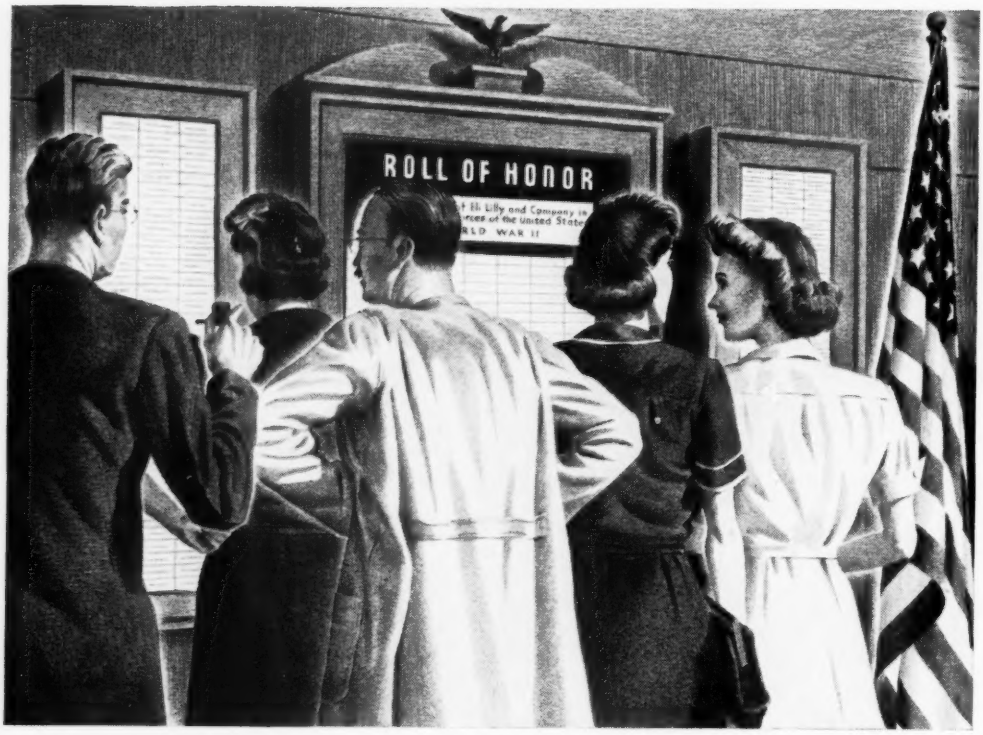

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A CONSIDERATION OF THE PRESENT STATUS OF THE SHOCK PROBLEM

"PROBLEMS ON SHOCKS"

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A RENEWED interest in shock is always manifested in time of war. It was during the Civil War that Mitchell, Morehouse, and Keen made observations which resulted in the publication of a paper which formed the basis for the vasomotor exhaustion theory of shock, the first of a number of theories in which the role of the nervous system was stressed. It was during the World War I that the first vigorous attacks on the pathogenesis of shock were made. Most of this work led to the formulation of the toxemia theory of shock, and the observations of Cannon, Bayliss, and Keith were outstanding. All of the work did not point in the same direction, as evidenced by the demonstration by Mann that traumatic shock cannot be produced by traumatization alone without opening of the abdomen, without the inducing of hemorrhage, or without injury to the medullary centers. It was during the first World War that the use of stored whole blood was suggested and employed on a small scale by Robertson, and that the use of blood plasma was suggested by Gordon P. Ward. A few cases of crush injuries and blast injuries were reported at this time, but the significance of these was not appreciated. It was shortly after this war that Hooker made his experimental observations on blast injuries and that Cannon wrote his book on *Traumatic Shock* which, though somewhat out of date, remains probably the best monograph on the subject.

The theory of traumatic toxemia remained essentially unchallenged for a number of years after the war, and it was then that several

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observers,[1, 2] using modifications of methods which had been employed previously, pointed out the important influence that the regional loss of fluid from the blood stream may exert in the causation of traumatic shock. These observations, which removed some of the obscurities regarding shock, encouraged surgeons to administer larger quantities of blood in the treatment of the injured. Blood banks were established in many hospitals. The use of blood plasma on a modest scale was introduced in a number of places. It was then that Elliott, Bond and Wright, Mahoney, Strumia, Levinson and others made their contributions, and the employment of plasma or serum on a larger scale resulted. Improvements in methods for processing plasma were being developed concurrently.

The theory which stressed the regional loss of blood and plasma as an important agent in the causation of traumatic shock gained many supporters during the five years preceding the present war, but has never been accorded the almost universal approval which the toxemia theory received after the last war. Credit is due Virgil Moon and John Scudder for continued interest in, and support and advancement of, the toxemia theory. At the same time, O'Shaugnessy and Slome and others reassessed the part played by the nervous system in traumatic shock and stated that it was an important one. Disagreements as to the pathogenesis of shock were lively but good-humored. In our enthusiasm for a particular method, few seemed to realize that the pathogenesis of all types of shock may not be the same.

This was, in brief, the state of affairs at the beginning of the present war, since which time vigorous attacks on the problems have been initiated by many investigators. The studies may be divided roughly into two groups: those on pathogenesis and those on therapy. Important advances have already been made, and it is likely that even more significant contributions will be forthcoming. From the viewpoint of the immediate war effort, the greatest accomplishment has been the collection and distribution of large quantities of blood substitutes.

No effort will be made to list the numerous contributions of those working in this field. An attempt will be made to indicate the general trend of the work both before and since the onset of war, and suggestions as to future problems will be offered.

THEORIES

Many theories regarding the cause or causes of shock have been advanced. If the term shock referred only to the traumatic type or types the situation would be complicated enough, but it becomes utterly confused when shock is used to designate a variety of conditions, many of which have no relation to one another. As Frank Mann and others have emphasized so often, *it is not a problem of shock but rather problems of shocks.* One of the most encouraging features of the work of the past

two years has been a growing appreciation by investigators of the fact that there are many causes of shock and that the mechanism of the production of all types of shock is not the same. A descriptive phrase should always accompany the use of the word shock, such as shock due to hemorrhage, shock due to burns, shock due to crush injuries, shock due to blast, shock accompanying infectious diseases, shock due to peritonitis, and so on. If the use of the term shock is restricted to failure of the circulation which accompanies trauma, there will still be confusion. For example, the mechanism of failure of the circulation following blast injury to the lungs is probably widely different from the mechanism of failure which results from a burn of a large surface of the body or from gross trauma to the extremities.

Speaking only of traumatic shock and admitting that there are exceptions, we may state that it is rather generally agreed that traumatic shock is usually due to either (1) regional loss of fluid, (2) toxemia, (3) nerve impulses, or (4) various combinations of these. These causes are placed in what I consider to be their order of importance, not in a case chosen at random but in the majority of cases. Furthermore, some instances of shock are due to other causes. For example, fat embolism is undoubtedly responsible for an occasional case of shock which follows trauma.

EXPERIMENTAL METHODS FOR PRODUCING SHOCK*

It would seem obvious that one should attempt to reproduce in the experimental animal a condition which is as closely analogous as possible to that which is encountered in an injured person. It is surprising, however, to note how often the experimental method has no apparent relation to traumatic shock as seen in man. Until recently, one could state that there is no proved relation between traumatic shock as observed in the human being and in animals. The brilliantly conceived and executed clinical studies of Cournand[3] and his co-workers at Bellevue and Presbyterian Hospitals have demonstrated that the circulatory system of man responds to trauma in a manner similar to that of the dog. This work allows one to speak with greater assurance regarding the value of experimental observations on this subject.

A constructive step in experimental studies would result from the placing of most of the emphasis on a few techniques for producing shock, in each of which an effort is made to cause a state of shock which can be reproduced with predictable morbidity and mortality. It might appear that this would be easy to accomplish, but such is not the case. There is wide individual variation in the tolerance of animals of the same species, even more pronounced in different species, to trauma as well as to hemorrhage. A recent personal experience has impressed upon

*I am indebted to Philip Bard, Robert Loeb, and Joseph Wearn for some of the ideas expressed in this section.

me again the difficulties of this work. George Duncan and I had performed a large number of experiments in which a mechanical crusher was applied to a posterior extremity for five hours. Anesthesia was maintained by the use of nembutal and morphine. The control as well as the experimental animals in which various forms of therapy were tried were kept in place on the table for approximately five hours after removal of the crusher. There were about forty control experiments and only one animal in this series survived. Recently, what appeared to be a slight alteration was made in the procedure because we were interested in following a therapeutic lead which was discovered elsewhere. The alterations in procedure consisted of using nembutal alone instead of nembutal and morphine, and in removing the animal from the table as soon as the crusher was taken off. A large proportion of these animals survived, and I believe it was due, in the main, to the fact that they drank water sooner and in larger quantities than was the case in the earlier studies.

In this same connection, Stafford Warren and his group in Rochester recently had an interesting experience. Using a crusher technique similar to that mentioned in the last paragraph, they had a mortality rate greater than 90 per cent. It became necessary for them to move to other quarters, and it was found there that most of the animals survived. It was noted that the room temperature in the new quarters was 10 to 15 degrees lower than it was in the original location. The temperature of the room was then elevated and the mortality rate rose to the original level. It is Warren's impression that this difference in mortality rates is explainable on the basis of variation in environmental temperature.

These experiences are mentioned in order to emphasize the difficulties of this type of experimental work. Whether the injured anesthetized animal lives or dies may be dependent upon some minor variation in the procedure. Studies on mechanism present difficulties, but it is especially hazardous to attempt to evaluate therapeutic procedures, the benefits of which are at best not very striking.

There are many other points regarding experimental methods which might be mentioned. Brief reference will be made to only a few of them. Anesthesia should be no deeper than is nesessary for the prevention of pain. If the blood pressure is obtained by cannulation of an artery and the employment of a mercury manometer, sodium citrate should not be used in the system. When the blood pressure falls, some of the citrate enters the blood vessels of the animal and death may result. Chlorazol fast pink is preferable unless studies involving dye determinations are being carried out. Animals should not be restrained on their backs on tables any longer than is necessary. This is a very abnormal position for a four-legged animal, and profound anesthetization of a

previously normal animal restrained on its back will usually result in death in several days.

Of the methods of producing shock now being systematically employed, the following seem to reproduce most closely the conditions encountered by the Armed Forces: (1) hemorrhage uncomplicated by gross trauma; (2) burns; (3) trauma to large masses of muscle; and (4) the re-establishment of circulation in a damaged ischemic area. Past and present work has indicated that at least three factors should be considered in any study of experimental shock. The first of these is a reduction in volume of effective circulating blood, usually due to regional loss of whole blood or plasma. The second is the elaboration of hypothetical toxic substances or the development of a metabolic derangement, local or general, which produces deleterious effects on the organism as a whole. The third is the role of the nervous system. Every experimental study of shock demands not only an awareness of these three factors but, as far as possible, a determination of their quantitative characteristics.

In shock produced by any of the four methods enumerated, the initial phases are certainly associated with and probably dependent upon a reduction in the volume of effective circulating blood. In any study of shock a failure to take this fact into consideration is bound to invalidate the significance of the results obtained. In studies which are undertaken to determine the value of therapeutic agents and in which the survival or mortality rates are equivocal, determinations of blood volume or cardiac output or both are imperative.

Investigations have indicated that at some time in the development of irreversible shock there appear effects which may be ascribed either to toxic substances elaborated in areas of tissue damage or to a derangement of metabolism produced by circulation which, either locally or generally, has been compromised over a long time. Although the evidence so far adduced bearing on this aspect of the subject has been vague, it is worthy of serious and intensive study. Such study requires the efforts of persons adequately trained in the principles of enzyme chemistry and tissue metabolism who will work in collaboration with investigators skilled in the techniques of producing shock experimentally and knowing the methods of evaluating its cause and severity.

Regarding the role of the nervous system, previous work has shown that the central respiratory and cardiovascular mechanisms tend to retain their functional integrity until the irreversible stage of shock develops. On the other hand, apathy and other signs of failure of certain higher nervous functions are commonly encountered in patients and unanesthetized animals before the irreversible stage develops. The theory that overactivity of the sympathetic system, especially the vasoconstrictor components, is an essential factor in bringing on shock has not received confirmation. There remains the hypothesis that afferent

impulses from traumatized tissue somehow produce shock or facilitate its development. No one has ever produced a prolonged state of shock simply by stimulation of afferent nerves. Although it cannot be denied that afferent impulses may be a factor in the genesis of shock, it does not seem likely that they are of major importance. Experiences with the use of spinal anesthesia in the treatment of injuries of the lower extremities of man have not been encouraging.

RECENT EXPERIMENTAL WORK ON PATHOGENESIS

It is my impression, and it is only an impression, that opposing schools of thought on the pathogenesis of shock are more nearly agreed at the present time than they were several years ago. Most of those who maintain that toxemia is the most important agent in the causation of traumatic shock admit that there may be other factors, and the same statement holds true for those who have stressed the importance of regional loss of fluid. This admission is a very hopeful sign.

The most remarkable shift of opinion has occurred in relation to the question of the permeability of the capillaries in shock. Previously, it was rather generally believed that the permeability of the capillaries throughout the body is increased in the terminal stages of traumatic shock, and many maintained that general capillary permeability is increased over normal in the early stages. The observations of a number of investigators, including Gregersen and Root, Fine, Gibson and Evans, E. I. Evans, Chambers, and others, indicate that there is not a general increase in permeability even in the fairly advanced stages. The following quotation is from a recent paper by Fine and Seligman[4]: "While the integrity of the capillaries may be impaired in the late shock phase, there is no evidence of a significant loss of plasma into tissues in untreated fatal shock following hemorrhage. Hence, an increase in capillary permeability is not a factor in the fatal issue. The phenomena which are set in motion by the initial critical loss in circulating plasma volume and which lead to death do not require that a progressive decline in plasma volume take place. Plasma loss into tissues therefore is not a crucial factor in hemorrhagic shock." Gibson and Evans, Fine and others, using radioactive substances, have obtained evidence that there is trapping of the red blood cells in shock. Even though I have been among those who have stressed the importance of a local increase in capillary permeability as contrasted with a general increase, it is difficult to accept without reservations the finding that there is not a general increase in capillary permeability in the late stages of shock.* It is to be hoped that the recent observations are correct for they make for a more hopeful outlook in therapy.

*Even if it be granted that there is no general increase in capillary permeability in untreated shock, it seems quite likely that general leakage may occur in the late stages if the capillary pressure is raised by the intravenous administration of fluids.

No attempt will be made to enumerate and describe all of the recent interesting observations. Some of these will be mentioned in a consideration of individual types of injuries such as occur in connection with so-called blast or crush. Since there has been a great deal of interest recently in the effects of ischemia, the experimental work of Root and Mann[5] will be described. Interpretation of their findings may be open to question, but it may be observed that attempts were made to determine the respective roles of (1) toxic effects, (2) sensory impulses, and (3) local loss of fluid. They state:

"The causation of the rubber band type of trauma was studied from three viewpoints: namely, as being due to (a) early toxic effects on the capillaries, (b) bombardment of sensory impulses from the traumatized region, or (c) local loss of fluid into the damaged region.

"a. Since large doses of histamine were necessary to cause death of the animal and also since histamine is removed rapidly from the blood stream of the rat, it would seem that histamine was not the causative factor in this type of shock.

"No immediate capillary dilatation was seen to occur in the mesentery or hepatic capillaries when the rubber bands were released. When the loss of fluid was minimized by wrapping the legs tightly, the capillary bed did not differ from that of the normal control animal over a six-hour period of observation following the cutting of the bands. Thus, there was no positive evidence for the liberation of a toxic substance causing immediate capillary damage in this type of shock.

"b. Section of the lumbar portion of the spinal cord with needling of the distal segment of the cord did not prolong the lives of the animals in the rubber band type of trauma and, therefore, the bombardment of sensory impulses from the traumatized region would seem to play a minor role in the causation of the type of shock.

"c. Wrapping the hind legs tightly with adhesive tape just before the rubber bands were cut, minimizing the local loss of fluid, did prevent the onset of shock as was confirmed by the normal respiratory rate, the normal capillary circulation, the general condition of the animal, and the normal results of hematocrit and red blood cell studies.

"Temporary wrapping of the legs for one hour after the bands were cut was not of any benefit."

The results of these experiments support the thesis that there is not a general increase in capillary permeability in shock. The observations are not in accord with those of a number of investigators who have presented evidence of the liberation of toxic products from an ischemic area or who attach great significance to the effects exerted by sensory impulses, such as Swingle.

A great deal of work on the relative importance of regional loss of fluid and of nervous impulses in the genesis of traumatic shock has been done by D. B. Phemister. His views on the subject appear to me to be

sound, and with his permission the following personal communication is quoted:

"From both clinical and experimental studies I believe that shock is rarely if ever produced primarily through the nervous system. However, if blood or blood and plasma loss as a result of trauma bring about a state of circulatory embarrassment, then a neurogenic lowering of blood pressure occurring simultaneously or afterward may still further lower blood pressure and be a secondary factor in importance in the production of shock. Psychic influences produced by pain or by the sight of a severe accident may cause fainting with a low blood pressure. But the reaction never lasts long enough to produce shock. The same is true of the fall in blood pressure in an abdominal operation in which there is no blood loss or obstruction of the return venous circulation, such as portal vein or inferior vena cava obstruction.

"Also marked lowering of blood pressure produced by the purely neurogenic procedure of stimulation of the carotid sinus or cardio-aortic nerves may be maintained for three or four hours without creating a state of shock. Release of the stimulus is followed by a return of pressure to the previous level and the animal usually lives on as if there had been no stimulation. Also traumatic stimulation of large wounds on the extremities by manipulation and pinching does not cause a reflex fall in blood pressure. It is only as the extremity swells from local blood and plasma accumulation that the blood pressure may be lowered. Stimulation of a cardio-aortic or carotid sinus nerve, maintaining a very low pressure for six to eight hours does create a state of shock which results fatally. However, it is so improbable that these special vasodepressor nerves would ever be stimulated in an accidental wound that the idea is scarcely worthy of consideration."

Recent observations on metabolic changes in shock are of particular interest. Govier and Greer[6] noted an elevation of pyruvate in dogs after hemorrhage. Significant changes in amino acid and carbohydrate metabolism have been found by Engel, Winton, and Long[7] in shock due to hemorrhage. It is suggested that the changes are due, "on the one hand to a decrease in hepatic function resulting from early anoxia of the liver, and on the other to the effects of anoxia on the peripheral tissues, causing an enhanced rate of protein breakdown and glucose utilization. In addition, the deficient oxygen supply results in an accumulation of lactate and pyruvate in the blood and tissues." The elevation of the amino acid nitrogen of the blood occurs only after the pressure has fallen to between 85 and 90 mm. of Hg, and hence this alteration cannot serve as an early index of shock. From the viewpoint of therapy, the experiments of Mylon, Winternitz, and de Suto Nagy[8] are at least suggestive. After having found that albumin is inferior to plasma as a blood substitute, they injected sodium succinate, in combination with other agents, because of the recognized influence it exerts

on the respiration of living tissue. Their preliminary observations indicate that sodium succinate is helpful in the treatment of experimental shock. Further studies of this nature are in order. An attack on the metabolic disturbances in shock would appear to be particularly hopeful and important.

PRODROMAL SIGNS OF SHOCK

It is well known by those who are interested in this subject that the the blood volume and cardiac output are usually diminished in traumatic shock before the arterial blood pressure declines significantly. Vasoconstriction can maintain an essentially normal arterial pressure for a fairly prolonged period when there is only a moderate decrease in the blood volume. When the arterial pressure declines in traumatic shock to the so-called critical level (approximately 75 mm. of Hg), it is a sign of advanced rather than incipient shock. It is much easier to prevent shock than it is to treat successfully the fully developed condition, and hence it would be highly desirable to have an early invariable criterion of shock which can be easily detected. It is unlikely that this hope will be realized, for there are few disorders in medicine in which a uniform early sign which is diagnostic is found. Nevertheless, work on prodromal signs is being continued.

In the present state of our information on the subject, the best plan is to treat or to prevent shock according to the nature and severity of the injury and the blood loss rather than to delay treatment until there is a decline in arterial blood pressure. This is the opinion of Whitby and associates,[9] of Grant and Reeve,[10] and of others who have examined a large number of wounded men in the present war. A rising pulse rate is often a useful indication of developing shock, but peripheral circulatory failure may exist when the pulse rate is 80 or less. A falling blood pressure is the best single index of progressing shock, but, as stated previously, it is not an early sign of traumatic shock. In injuries such as burns, where the loss of fluid is restricted in the main to plasma, an increase in the concentration of the red blood cells may serve as a helpful early sign. With the exception of patients with burns and crush and blast injuries, early hemoconcentration has not been the usual finding in the present war. Frequent but not unvarying signs include cold extremities, sweating, thirst, pale mucous membranes, and diminished pulse volume.

A number of factors influence the response of the body to injuries. Inadequate food and water, chilling or excessive heat, physical and emotional exhaustion decrease the tolerance to trauma. Under such circumstances it is particularly important to institute early treatment.

CLINICAL OBSERVATIONS

During the present war there have been numerous obstacles to the making of clinical observations on a large scale. The nature of mobile

warfare is such that one cannot predict with any degree of certainty the localities in which injuries will be encountered. Distances are great and the transportation of apparatus presents difficulties.

A number of obstacles also have been encountered in the study of shock in the civilian population in this country. Preventive measures such as the use of whole blood and plasma have reduced greatly the incidence of shock in association with accidents and operations. Because of restrictions on the use of the automobile and a lowering of the speed limit, the number of accidents has decreased very decidedly. Studies on the injured in defense industries have not appeared advisable because they might result in a little delay in carrying out therapeutic procedures. A reduction in the personnel of the professional staffs of most institutions has increased routine duties for those who remain and there is little time for such investigations.

Despite these obstacles, some progress has been made, and an outstanding example is the work of the group at the Bellevue and Presbyterian Hospitals in New York. Reference[3] has been made to their careful studies on the circulatory system of the injured man.

No attempt will be made to discuss all types of injuries. Some of the important observations on multiple wounds of soft parts, burns, and crush and blast injuries will be discussed briefly.

Multiple Wounds of Soft Parts.—Kekwick, Marriott, Maycock, and Whitby[9] made a careful study of twenty-four patients who were severely injured. They stated that the decrease in the blood volume in these patients could be accounted for by external loss and by extravasation into the injured area, and that there was no evidence to suggest loss of plasma in regions remote from a seat of injury. There are two important facts that emerge from this study as well as from the careful clinical report of Grant and Reeve.[10] These facts were known already but they needed to be emphasized. The first of these is that a decline in blood pressure is a late rather than an early sign of traumatic shock. All of these investigators noted further that the cardinal symptoms of shock may be present without much hemoconcentration or hemodilution and that the pulse rate is an unreliable indicator. It is emphasized that patients should be treated according to the nature and severity of injury and blood loss and that one should not wait for alterations in measurable functions of the circulation. The second point of importance is that enormous quantities of whole blood or plasma may be required for the successful treatment of those with severe injuries. Blood pressure determinations are of value in estimating the response to treatment. Whitby and his associates state that, as a rule, a rise of 10 to 20 mm. of mercury can be anticipated for every 540 c.c. transfused, if bleeding has ceased and no other causes of loss of circulating plasma are operating.

These reports and some others which will not be mentioned present clinical evidence of the important part which regional loss of blood and fluid may play in the development of shock. A question will be raised here which could probably be considered more appropriately under burns. Do severe injuries usually cause a serious interference with the blood supply to the part (ischemia), and if so, does the ischemia result in damaging effects to the general circulatory system? Further information on these points is needed. Severe injuries such as burns cause death of some tissues; structures well beneath a burned area probably have an entirely adequate flow of blood. Further information is needed regarding the state of the circulation of the zone between the devitalized area and the essentially normal one. It is likely that the flow of blood is considerably reduced and this may result in the passage into the circulation of toxic products.

Burns.—There is little difference of opinion regarding the general treatment of patients with burns. It is agreed that enormous quantities of plasma may be lost from the circulation and that treatment should include the intravenous administration of large amounts of plasma. Furthermore, the extent of the surface that is burned, the increase in the concentration of the red blood cells, and other definite measurements serve as good indices of the quantity of blood substitute that is needed. Elkinton, Wolff, and Lee[11] have observed in patients that the loss of injected plasma is more rapid during the early stages after the burn than it is subsequently. If the available supply of plasma is limited, an appreciable proportion of the total should be saved for the period of beginning twenty-four hours after the burn when the local leakage will have diminished.

Rhoads and Lee and others have found in patients that the use of tanning agents causes a reduction in loss of fluid from a burned area. It is likely that the same effect can be brought about by the employment of pressure dressings. One of the most interesting alterations in viewpoint in the present war has been the trend away from the use of tanning agents in the local treatment of burns.

The two important problems in the treatment of burns are the restoration and maintenance of an adequate blood volume and the prevention of infection. It should be remembered that the volume of the blood substitute as well as its protein content is important. If concentrated albumin is used in treatment in the early period after a burn, preferably it should be diluted with or administered simultaneously with normal salt solution. A vigorous effort should be made to maintain adequate urinary output. It is very helpful if the patient can retain fluids which are taken by mouth. In any case hemoconcentration is usually replaced by anemia and hypoproteinemia four to six days after a severe burn, and the injection of whole blood is then indicated.

Crush Injuries.—A few instances of crush injuries were observed in World War I, but the condition seems to have escaped further attention until the beginning of the present conflict. As a matter of fact, it may very well be that the importance of the condition has been overemphasized since only about seventy-five cases have been described. The usual story which is given is that a person is pinned by falling debris. On discovery several hours after, the patient appears to be in very good condition, if only an extremity is pinned, and is released. Swelling of the extremity ensues and the patient may present evidences of shock. This condition usually responds promptly to adequate intravenous therapy. The patient may be thought to be on the road to recovery when several days later oligemia, uremia, and death ensue. Death is believed to be due to renal failure.

A proper understanding of this condition has been retarded by the inability of investigators to reproduce the delayed renal failure experimentally. It would appear that the renal damage in man is due to some cause as yet unascertained, such as associated disease or infection, or that man and dog differ in their response to ischemia superimposed on trauma. In my opinion the main value in the reports lies in the attention which has been focused on the effects of ischemia, and particularly that which accompanies gross trauma. It would seem that it is in such conditions that one is most apt to be able to demonstrate toxic products. Furthermore, a renewed interest in renal function in shock has been stimulated.

Many suggestions have been made regarding the treatment of patients with crush injuries. Recent recommendations by Bywaters[12] are as follows:

"The natural tendency under emergency conditions is to treat shock first, then the local limb condition, and lastly the renal failure on or about the third or fourth day, when signs of renal damage are obvious. Since it is possible that the renal damage occurs soon after the reestablishment of an adequate blood supply to the damaged limb, these three aspects should be considered in the reverse order.

"1. Ample alkaline fluid (3 liters daily), by mouth preferably, or by rectum, intramuscularly or intravenously, must be given rapidly at the earliest possible moment, to produce an alkaline diuresis. If possible, this should be done while the patient is still trapped under the wreckage. We favour for ingestion an alkaline fluid flavoured with citrus juice or peppermint and glucose, containing sodium citrate and sodium bicarbonate, 2 g. of each to the ounce. Coffee or tea is also useful, and morphine should be given if required. For intravenous injection, isotonic sodium citrate (3.8 per cent) or sodium lactate (M/6) should be used. Enough alkali should be given to make the urine alkaline: This will mean probably 30 to 40 grams daily or more by mouth, or a lesser

quantity by intravenous injection. If tetany is induced, calcium gluconate should be given intramuscularly. Potassium salts must not be used. Sodium sulphate (2 per cent) may also be injected intravenously in combination with the above measures to maintain urinary output.

"2. With the kidneys thus protected, it is safe to restore the circulation by combating shock, if this is present. Plasma or serum should be given, or, if there has been much hemorrhage, blood. A large quantity may have to be administered: So long as the arterial blood pressure remains low no harm need be feared. Saline is of no value. Overheating the patient is dangerous."

This point of view is a very interesting one, and it would certainly seem that Bywaters is correct in his contention that diuresis should be stimulated. On the other hand, it would appear that impending shock should be treated concurrently by the intravenous administration of blood plasma.

Blast Injuries.—No attempt will be made to enumerate separately the findings of Hooker, of Zuckerman, of Denny-Brown, and of others, but the recent paper by Williams[13] will be reviewed in moderate detail. The pressure exerted by an exploding bomb may be tremendous. There are three components in the blast wave in *air:* (1) positive pressure wave acting directly on the chest and indirectly on the lungs through the diaphragm; (2) negative air suction wave; and (3) the mass movement of air or gas (windage factor). The mechanism of action of blast in *water* is somewhat different in that, generally speaking, only the primary positive pressure wave is of importance. Blast at an equal distance is more dangerous in water than in air because the rate of fall in pressure is much more rapid in air. This statement has to be modified somewhat if air blast occurs in the vicinity of rigid objects such as the walls of a building which will cause the pressure to be built up by reflection. Other parts of the body (abdominal contents, tympanic membranes, etc.) as well as the lungs may be injured by blast. Williams made the following statements concerning the mechanism of blast in water. "Now consider the human body, which has roughly the same density as water. When the pressure wave impinges on the body there will be no reflection, but the pulse will be transmitted through the tissues without displacement, just as if the body were so much water. However, when the transmitted pulse encounters an air cavity in the body, e.g., the lungs, the same phenomenon will occur as has been described above; that is, the static wave of pressure will change into a wave of kinetic energy in the layers of tissue lining that cavity and a disruptive effect will occur. Hence it can be understood that the lungs and other gas-filled cavities in the body are particularly susceptible to damage from the pressure wave, even though the body itself may not be deeply immersed."

An excellent dissertation on clinical immersion blast was presented in the issue of the United States Naval Medical Bulletin for January, 1943. In confirmation of previous observations, it was found that the severity of symptoms depended on the distance of the men from the source of the explosion and on their position in the water, whether horizontal or perpendicular, whether facing the blast or with their backs turned. On physical examination abnormal chest signs were more often absent than present, but roentgenograms revealed in all but one case out of a total of thirty-five slight to moderate areas of increased density at one or both bases. Severe intraabdominal lesions were present in a number of cases. The Naval observers conclude that the principal seat of trauma in atmospheric blast is in the thoracic cavity, whereas the predominating injuries in immersion blast are abdominal.

There is wide variation in the early signs and symptoms which may follow blast injuries as illustrated by the following example given by Williams. "Seven men on board of one of H.M. ships were in the vicinity of a magazine hatch when the ship blew up. These men managed to reach shore, but one of them felt so ill that he was unable to stand and had to be carried by his comrades to shelter in a school, where the party turned in for the night. The sick man was horrified to wake the next morning and see the remaining six men lying with rather blue faces and to be informed that they were all dead." Zuckerman found that some animals were able to run about for some time after exposure to blast.

In only four of 1,500 casualties mentioned by Williams were there internal blast injuries without external marks of violence. Patients with blast injury of the lungs usually have pain in the chest, difficulty in breathing, and a grunting cough. The cough is at first unproductive but later there is bloodstained sputum. Moderate cyanosis is usually observed. Although the clinical picture of "blast abdomen" varies greatly, there is usually abdominal pain, tenderness, and rigidity.

Aluminum suits lined with rubber have been shown to be effective in protecting against moderately severe pressure waves. They are, however, too expensive and cumbersome for general purposes. An inflated rubber jacket affords some protection. It is important to protect the abdomen as well as the chest. As stated previously, men swimming on their backs at the time of a blast are less apt to be injured severely than are those in the opposite position.

If shock results from the injury, it may be necessary to administer plasma, but this should be avoided if possible because pulmonary edema, if present, may be increased. Blast injuries of the lungs should be treated by rest, sedatives, the inhalation of high concentrations of oxygen, and respiratory isolation. Most patients who are suspected of having blast injuries of the abdomen recover without surgical intervention,

but all such patients should be followed closely for evidence of perforation of hollow organs or continued bleeding.

PREVENTION AND TREATMENT

Although much remains to be learned about the pathogenesis and treatment of shock, the available information about most types is not meager. A good job has been done in disseminating information but the efforts need to be increased. Civilian as well as military authorities on the subject should visit the various Army and Navy stations and should discuss the problems. There should be even more practice in the use of blood substitutes as contained in the Army and Navy packages. All medical officers should be thoroughly familiar with methods for grouping and matching blood.

Crystallization of opinion regarding the effectiveness or noneffectiveness of several agents has resulted from recent work. The value of adrenal cortical extract has been investigated very thoroughly, and it is agreed by most of the workers that it is not effective in the treatment of shock. The possibility remains that cortical extract may be helpful several days after injury when "adrenal exhaustion" may have occurred. If the observations to the effect that capillary permeability in traumatic shock is not increased are correct, then the theoretical reasons for the use of cortical extract are removed.

Regarding the value of the inhalation of high concentrations of oxygen there is some difference of opinion, but most of the observers are agreed that the benefit is slight. The oxygen saturation of the arterial blood is normal in most instances of shock. Difficulties of transporting containers of oxygen militate against the wide use of this agent of doubtful value.

In the absence of intracranial injuries, pain should be mitigated by morphine. Patients who are in shock rarely complain of pain, and the administration of large doses of morphine is a mistake. It is my opinion that one should not give as much as ½ gr. in a single dose even to the patient who is having pain. Morphine may cause nausea and vomiting which will further deplete the body of fluids. Moreover, the respirations may be unduly depressed. It is probably better to give ¼ gr. of morphine and to repeat this dose if necessary.

The head-down (shock) position is advisable for most patients with falling or low blood pressure. This position is not indicated for those with chest injuries, pulmonary edema, and head injuries.

It is fortunate that there is a growing appreciation of the dangers of the indiscriminate use of heat in the treatment of shock.[14] Too much heat is dangerous because it causes loss of fluid through sweating and inhibits the normal vasoconstrictive defenses of the body. The reduced blood volume in traumatic shock may be adequate to meet temporarily the requirements of the more vital structures such as the heart, the

brain, and the adrenals, but may be entirely inadequate if vasoconstriction in the extremities is replaced by vasodilatation as a result of the application of heat. An effort should be made to conserve body heat in the injured person who has been exposed to cold, but such a person should be covered with blankets rather than treated by surrounding him with hot-water bottles. When the patient has been placed in warm surroundings and when the deficit in blood volume has been repaired by appropriate therapy, the temperature of the extremities will usually return gradually to normal.

Since the major single cause of shock seems to be a decrease in the volume of the circulating blood, treatment is based on checking such loss and replacing body fluids by the best means at hand. Measures which may be effective in the early stages may not result in sustained improvement at a later time.

Hemorrhage should be controlled as quickly as possible, preferably either by ligating a bleeding vessel or by pressure. The use of a tourniquet on an injured extremity should be avoided whenever possible. If it is unavoidable, several points should be borne in mind. The tourniquet should be placed as low as possible on the limb. If a means for cooling the part distal to the tourniquet is available, this should be done in order to reduce the nutritional requirements and the production of metabolic end products. The temperature should not be lowered below 50° F. or 10° C. If a limb is hopelessly mangled, a tourniquet should be applied just below the site of election for amputation and should be left in place until the extremity has been removed.

Fluid administration, including the use of blood and blood substitues, is the single most effective means of treatment. Water should be given by mouth if not contraindicated and if tolerated. If water is not retained, hot tea or coffee should be tried.

While salt and glucose solutions are excellent for the correction of dehydration, their use does not usually result in sustained improvement in the treatment of shock. The intravenous injection of large quantities of solutions of crystalloids in the presence of gross capillary damage may result in harmful[15] rather than beneficial effects.

The main reliance in preventing and treating shock is the use of adequate quantities of whole blood, plasma, or albumin. Unless pulmonary edema is suspected, blood or a substitute may be given as rapidly as one pint of isotonic fluid in ten minutes. If the desired effect is not obtained in fifteen minutes, the dose should be repeated. Whole blood is preferable to a substitute if there has been massive hemorrhage, but plasma should be given in the meantime if delay is entailed in the use of whole blood.

The initial injection of a blood substitute may be two units of reconstituted plasma or its equivalent, one unit (25 Gm.) of concentrated

albumin. Since a significant elevation in the blood pressure usually accompanies the administration of a relatively small volume of concentrated albumin, an effort should be made to attain as adequate hemostasis as possible before the albumin is given. Since the concentrated albumin draws fluid from the tissue spaces into the blood stream, dehydrated patients should be given additional water and salt. When normal salt solution is available, the concentrated albumin may be diluted in the ratio of two units (50 Gm.) to a liter of the salt solution. It seems advisable not to give more than ten units of albumin in a forty-eight-hour period.

Simple dehydration collapse in the absence of injuries is treated by cooling the patient and by giving salt solution by mouth. The fluid should be given intravenously if it cannot be taken by mouth. As soon as sweating stops, one should proceed cautiously in efforts to reduce an elevated temperature.

It would appear to be desirable to make some of these recommendations more specific. Such a procedure is difficult, however, in view of the great variation in conditions of all kinds to which the fighting forces are exposed.

UNSOLVED PROBLEMS

It is the opinion of some that little is known about shock and that the major problems are unsolved. Such persons must find it difficult to explain why traumatic and postoperative shock are encountered so infrequently today in the civilian practice of surgery. As stated previously, it is my contention that a great deal of useful information is available at present. At the same time, there are many unsolved problems, and a few of them will be mentioned and discussed briefly.

Pathogenesis.—1. There is need for further search for and identification of a toxic factor or factors. It follows that there should be efforts to find an antidepressor substance or substances. It is my opinion that this is the number one problem since the results of regional loss of fluid can be combated fairly effectively by the use of blood and blood substitutes. All such studies should take into account this loss of fluid. It should be emphasized that the important point is to identify the depressor substance or substances rather than simply to perform experiments the results of which suggest that toxic products are present. Recent work seems to show that the so-called toxic substance may be simply a disturbance in tissue metabolism.

2. There should be additional studies on the nervous factors in various types of shock. It would seem that the therapeutic implications which might emanate from such studies would not be so great as those which might result from work on depressor and antidepressor substances. The results which have attended the blocking of the nerve supply of an injured area have not been very encouraging.

3. The recent observations to the effect that there is not a general increase in capillary permeability even in advanced shock should be confirmed or denied. If it is true that red blood corpuscles are trapped, it should be determined where they are trapped. If chiefly red corpuscles are trapped, where is the plasma? A particular effort should be made to determine whether the capacity of the venous system is greatly increased.

4. The role of ischemia in the causation of shock should be further elucidated. Ischemia of various organs as well as of skeletal muscle should be studied.

5. There is suggestive evidence that in some types of shock there is loss of ability to restore plasma volume by withdrawal of fluid from the tissues. Further work on this subject should be undertaken.

6. It is rather generally agreed that the heart usually is not at fault in the genesis of early shock. The work of Wiggers and others suggests that its function may be impaired in later stages. More work should be done.

7. Much remains to be learned about renal function in various types of shock. The cause of renal failure in some instances of crush injuries and burns should be determined. Fortunately, a number of competent investigators are working on this subject.

8. The terms reversible and irreversible are often used in designating the stages of shock. What occurs that changes the reversible to the irreversible stage and what signs, if any, indicate this alteration? Some information on this subject is available but more is needed.

9. Further studies on the effects of alterations in body temperature, local and general, in the pathogenesis of traumatic shock should be made. The effects of lowering the general body temperature in the presence of fever resulting from infection should be investigated.

10. Very little is known about the influence which infection, superimposed on injuries, exerts in the pathogenesis of shock. This is a difficult problem to approach but information is urgently needed.

11. There seems to be little doubt that fat embolism is responsible for an occasional case of shock. Further clinical observations should supply additional information on this subject.

PREVENTION AND TREATMENT

The following are a few of the many subjects on which additional information is needed:

1. If blood is trapped, can a means be found for restoring the trapped or segregated blood to active circulation? If there is an excess of blood in the veins, is there a mechanical means by which its return to the heart can be facilitated?

2. Do substances such as hypertensin exert a beneficial effect in the treatment of shock? The preliminary observations of Ogden, Collins,

Dexter, Braun-Menendez, and others on hypertensin in this connection are interesting.

3. Although it is agreed that adrenal cortical extract is not effective in the prevention or treatment of shock, except in adrenal insufficiency, does the use of adrenal extract accomplish good several days or longer after injuries when adrenal "exhaustion" may have occurred?

4. Should injured areas (burns, etc.) be cooled? If so, what degree of cold is optimal? A simple method for cooling an injured extremity, particularly one to which a tourniquet has been applied, is needed. This problem might appear to be an easy one, but actually under most conditions of warfare it is very difficult to cool a part by artificial means.

5. What quantity of blood or blood substitute is needed and at what rate should the fluid be administered? It is obvious that the answers vary from case to case, depending upon the nature and severity of the injury. The quantity required in the treatment of burns is relatively easy to determine, for it may be estimated from the extent of the burn or the increase in the concentration of the red blood corpuscles or hemoglobin content. The problem is not so simple in those injuries in which there is a loss of red blood cells as well as plasma. A rapid uncomplicated method for determining the blood volume or the state of hemoconcentration or hemodilution on the battlefield would be very helpful.

6. Concentrated human albumin presents the advantages over liquid blood plasma of easier preservability and transportability, but is albumin as effective as plasma in the prevention and treatment of shock? Clinical experiences with albumin have been very gratifying, but some of the experimental work indicates that it is inferior to blood plasma. Further investigation of the subject is needed.

7. How much blood or plasma in which sodium citrate is used as the anticoagulant may be given with safety in a short period of time? The recent work of Ivy and his associates[16] shows that there is a limit beyond which the citrate produces marked disturbances.

8. Is it possible to obtain a fraction of animal plasma which is nonantigenic for man? Much work is being carried out on this subject.

9. Can the quantity of plasma that is necessary in the treatment of shock be reduced by the use of amino acid mixtures? A number of investigators, including, Elman, Brunschwig, and Whipple, are advancing our knowledge on this and other questions.

10. The widespread use of plasma has resulted in the discarding of enormous quantities of red blood corpuscles. Is there some need for which these corpuscles or fractions of them could be utilized?

11. Are there substitutes not of animal origin which are as effective or almost as effective as plasma in the treatment of shock? None has been found as yet, but an intensive search continues by various groups.

12. Are thiamine and vitamin C, in the absence of vitamin deficiencies, helpful in the prevention and treatment of shock? Is it possible to sup-

ply substrates which will aid in the correction of disorders in metabolic processes? If the hypothetical toxic substances are simply the results of disorders in tissue metabolism, can a method be found to correct the abnormalities? The enzyme systems in shock should be carefully investigated.

13. The question frequently has been asked whether it is possible to "precondition" men in dangerous military zones in order to lessen the chances of the development of shock if injury should occur. Is it possible to have a reserve storage of fluid in the body tissues? In particularly dangerous times, is the oral administration of normal salt solution or glucose indicated? The answers to these questions have not been supplied.

14. Is there some way to prevent the nausea and vomiting which are usually part of the shock picture? If we assume that a significant part of the fluid taken by mouth would be absorbed, the abolition of nausea and vomiting would be a great advance in therapy. It is much more desirable to give nonprotein-containing fluids by the oral route, unless contraindicated, than by the intravenous one.

15. In the treatment of crush injuries should one attempt to cause an increase in urinary output by the administration of fluid by various routes before one treats the impending shock by the injection of blood plasma? Should a tourniquet be applied and amputation performed as soon as possible in those instances in which an extremity has been pinned longer than several hours? Much remains to be learned about crush injuries.

16. In regard to "position" in shock, how much should the head be lowered and how long should this position be maintained? It is agreed that the head-down position is indicated for most patients in shock except for those with brain and pulmonary injuries.

17. What is the best anesthetic to employ in the treatment of the severely wounded? Local infiltration is safest but frequently is inadequate. Most observers agree that anesthetic doses of intravenous barbiturates and of agents injected into the spinal canal are dangerous for these patients. Cyclopropane and ethylene are usually not available. Nitrous oxide should not be used except for very brief procedures. As emphasized by Bartlett and Evans, intercostal nerve block lessens the dose of the general anesthetic agent that is required for abdominal operations. Ether, though presenting some disadvantages, remains among the safest of the agents for inhalation. Possibly the dangers in the use of chloroform have been overemphasized. The probable ill effects of this agent should be reinvestigated. The situation regarding the choice of anesthetic agents for the treatment of shock needs clarification.

18. How much morphine should be given to an injured person? Should not a distinction be made in dosage according to whether or not

the patient is in shock? Patients in shock rarely complain of severe pain. Is morphine responsible for some of the nausea and vomiting that often accompanies shock? It is my impression that, except in unusual circumstances, it is unwise to administer as much as ½ gr. of morphine in a single dose.

19. Is it not possible to provide more adequate protection against injuries in the military forces? Is it possible to devise a more effective means for cushioning the pressure wave of water blast? Should protective chest and abdominal armor plates be used more extensively? Can the hazards of burns on ships be lessened by alterations in the type of clothing that is worn? The value of adequate covering of the skin has been demonstrated in the case of flash burns.

20. With the knowledge that the ideal treatment of penetrating abdominal wounds is immediate operation, but that this is impossible in some of the forward areas, is there some nonoperative means which will result in a greater saving of lives than at present? This is one of the most important problems confronting military surgeons.

21. A number of miscellaneous questions might be asked. Is the available information on the pathogenesis, prevention, and treatment of shock being conveyed effectively to the men, usually battalion medical officers, who will actually treat the injured? Should there be teams composed of military and civilian surgeons who could instruct the physicians and their assistants in the various camps? If so, there should be demonstrations of the use of blood substitutes as contained in the Army-Navy packages. Should there be a number of men in the services who specialize in intravenous therapy, including blood grouping and matching? In the short time available, are our students and house officers getting adequate instruction in the treatment of the various types of injuries that are encountered in warfare? Could a more adequate description of the medical problems which are met in the various fighting zones be sent to designated centers in this country in order that instructors and investigators could carry out their duties more intelligently? One realizes, of course, that total mobile warfare presents many impediments to the adoption of routine methods of therapy and to the wide dissemination of information.

CONCLUSIONS

There are many types of shock, and we are dealing with "problems of shocks rather than the shock problem." The most commonly encountered etiologic agent in the genesis of traumatic shock is the regional loss of plasma or whole blood from the blood stream. There are many unsolved problems, some of which have been considered, but the available information is such that the majority of instances of traumatic shock can be prevented or treated successfully if advantage is taken of existing knowledge.

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THE EFFECT OF INFUSIONS OF BOVINE SERUM ALBUMIN IN EXPERIMENTAL SHOCK*

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THE search for an adequate and readily available substitute for blood in the treatment of traumatic shock has led to the preparation of purified fractions of plasma proteins of both human and animal origin.[1,8] Such preparations appear to have certain advantages over blood or plasma in that they are more readily preserved or transported and, with respect to animal fractions, are unlimited in source. This study was undertaken to determine the efficacy of bovine serum albumin in experimental shock. Particularly severe thermal trauma, involving one-third or more of the total body area in dogs, was selected as a means of producing shock because extensive observations on the effects of treatment in this type of injury in human beings are difficult to obtain.

The course of the changes in hematocrit, plasma volume, plasma protein concentration, pulse rate, and blood pressure following thermal trauma in dogs has been described previously.[5, 9] Although there is some variation in individual animals, in general the course of this type of shock is sufficiently uniform to permit an evaluation of therapeutic procedures. The characteristic changes in untreated dogs are depicted in Fig. 1. There is a rapid reduction of plasma volume with marked hemoconcentration, followed by a continued but more gradual change in the same direction. The concentration of plasma proteins at first increases slightly, then falls moderately, but from the onset there is a marked reduction of total circulating protein. An initial fall of mean arterial blood pressure followed by a rise, sometimes above the preexisting level, which is maintained until just before exitus, is the rule. The pulse rate rises early and shows a progressive upward trend, being above 200 toward the end of the experiment. Pathologic examination of the animals sacrificed early in the experimental period discloses very little variation from the normal, but in animals which die or are sacrificed late, that is after seven to fifteen hours, microscopic changes similar to those described by Moon[10] are consistently present.[5]

The effects of various forms of replacement therapy on the plasma volume, circulatory changes, and pathologic findings under the conditions of these experiments have been described before.[4] It is sufficient

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to state here that when a continuous infusion of normal or slightly diluted plasma is given in amounts of 75 to 100 c.c. an hour, depending on the size of the animal, the plasma volume and peripheral circulation are well maintained and there is a striking amelioration of the usual tissue changes of advanced shock. The points which seemed desirable to determine in this study were:

1. Is bovine serum albumin toxic to dogs when injected after an injury which involves extensive tissue damage?

2. Does bovine serum albumin remain in the circulation sufficiently long to maintain plasma volume?

3. How effectively, in comparison with plasma, will bovine serum albumin limit the circulatory and pathologic changes which follow severe burns?

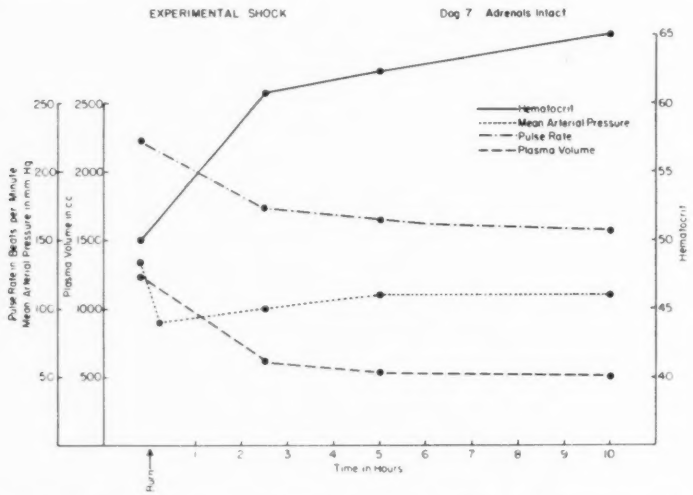

Fig. 1.—Changes in plasma volume, hematocrit, pulse rate, and mean arterial pressure in shock due to burns, untreated. Animal sacrificed at ten hours.

EXPERIMENTAL PROCEDURE

Mongrel dogs were used in all the experiments. A splenectomy was performed several weeks prior to the crucial experiment because previous observations in dogs indicated that otherwise the activity of the spleen caused wide fluctuations in the hematocrit with little relation to changes in red cell volume. The animals were given water liberally but no food for twenty-four hours before the experiment. Anesthesia was induced with sodium pentobarbital in doses of 32 mg. per kilogram of body weight and maintained throughout the experiment by small supplementary injections as needed. The possible disadvantages of this agent as an anesthetic have been discussed previously and the effects of the drug in control animals described.[5]

The mean arterial blood pressure was recorded by means of a mercury manometer connected by a cannula with the right femoral artery. At

frequent intervals, the pulse rate was counted at the apex of the heart by means of a stethoscope, as well as being recorded on the kymograph. The respiratory rate was also taken frequently. The plasma volume was determined by the direct method of Gibson and Evans,[6] a reinjection of dye being made for each determination. The plasma proteins were determined by the micro Kjeldahl method. The prothrombin time was determined by the method of Quick.[12]

All samples of blood were taken from the jugular veins which were exposed for this purpose but protected by sponges moistened in saline solution. All infusions were given through the left femoral vein which was cannulated for that purpose.

The fractions of plasma proteins employed in these investigations were prepared by E. J. Cohn, W. L. Hughes, Jr., L. E. Strong, and their colleagues in the Harvard Plasma Fractionation Laboratory in collaboration with J. D. Porsche and his colleagues in the Armour Laboratories. As this study progressed, increasingly pure preparations of bovine serum albumin were made available. In the later experiments a solution of crystallized bovine serum albumin was used. This proved so much more efficacious that certain opinions based on the earlier studies had to be revised. However, all the experiments are included in this report.

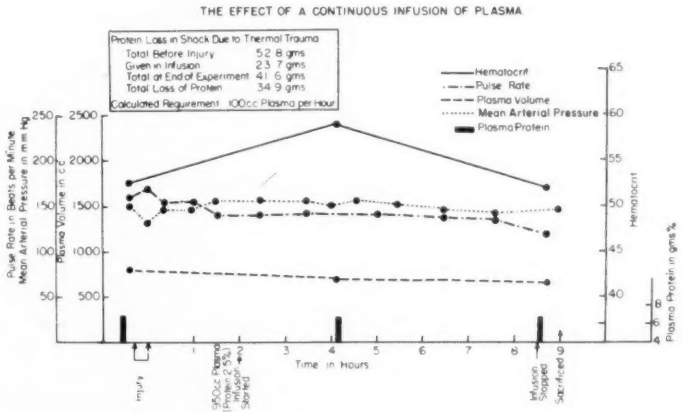
THE EFFECT OF A CONTINUOUS INFUSION OF PLASMA
Protein Loss in Shock Due to Thermal Trauma
Total Before Injury 52.8 gms
Given in Infusion 23.7 gms
Total at End of Experiment 41.6 gms
Total Loss of Protein 34.9 gms
Calculated Requirement 100cc Plasma per Hour
Hematocrit
Pulse Rate
Plasma Volume
Mean Arterial Pressure
Plasma Protein
Pulse Rate in Beats per Minute
Mean Arterial Pressure in mm Hg
Plasma Volume in c.c.
Hematocrit
Plasma Protein in gms %
Time in Hours
Injury
950cc Plasma (Protein 2.5%) Infusion Started
Infusion Stopped
Sacrificed

Fig. 2.—Continuous infusion of plasma in amounts equal to the stipulated requirement maintained plasma volume and mean arterial pressure satisfactorily.

The results are given in Table I. In the early experiments in which comparatively crude preparations were used, the results although by no means comparable to the effects of plasma, were encouraging in that they demonstrated that a heterologous albumin fraction remained in the circulation sufficiently long to maintain plasma volume for several hours and did so apparently without a notable toxic reaction. This was especially impressive when the experiment was of short duration as in Nos. 1, 3, and 4. In the longer experiments, Nos. 2 and 5, the results

TABLE I

EXPERIMENT NO.	DATE	WGT. (KG.)	TYPE OF THERAPY	TIME	PULSE RATE PER MIN.	MEAN ARTERIAL PRESSURE (MM. HG)	RESPIRATORY RATE PER MIN.	HEMATOCRIT (VOL. %)	PLASMA VOLUME (C.C.)	TOTAL PROTEIN (GM. %)
1	4/14/41	15.3	Amorphous bovine serum albumin, 350 c.c. by continuous intravenous infusion at 50 c.c. per hr. for 6 hr. started ¼ hr. after injury	Before injury	200	145	10	50.0	840	6.3
				¼ hr. after injury	220	140	--	53.1	---	7.0
				4 hr. after injury	156	144	14	50.8	---	6.3
				5¼ hr. after injury	130	150	20	48.6	---	6.8
				6¾ hr. after injury	130	145	16	47.8	670	6.0
2	4/24/41	18.6	Amorphous bovine serum albumin, 500 c.c. (25 Gm.) in 4 hr. Started 10 min. after injury	Before injury	175	130	7	47.7	926	6.5
				10 min. after injury	170	60	24	53.0	---	--
				4 hr. after injury	250	140	28	42.6	770	6.4
				8 hr. after injury	250	110	36	41.0	800	6.0
			500 c.c. (25 Gm.) in 3 hr. Started 5 hr. after injury							
3	5/22/41	20.0	Amorphous bovine serum albumin, 460 c.c. (20.4 Gm.) in 5½ hr. Started 10 min. after injury	Before injury	135	136	4	47.0	1440	7.1
				10 min. after injury	138	125	3	56.5	----	7.2
				2 hr. after injury	120	140	6	51.5	----	6.7
				6 hr. after injury	100	135	3	47.5	1140	6.9
4	5/27/41	15.4	Amorphous bovine serum albumin, lot 10-11, 350 c.c. (11.0 Gm.) in 5 hr. Started 20 min. after injury	Before injury	160	110	6	47.4	637	5.8
				10 min. after injury	172	118	3	53.5	---	7.0
				3 hr. after injury	170	130	20	46.0	---	--
				5 hr. after injury	190	120	24	39.2	500	5.9
5	6/12/41	19.3	Amorphous bovine serum albumin, lot 16, 750 c.c. (37 Gm.) in 8 hr. Started 30 min. after injury	Before injury	180	115	6	43.1	1120	6.0
				15 min. after injury	167	110	10	49.0	----	6.8
				4½ hr. after injury	170	105	18	37.4	965	5.3
				8¼ hr. after injury	190	100	40	31.0	1265	5.2

6	7/ 1/41	23.5	Amorphous bovine serum albumin, lot 17, 360 c.c. (17.6 Gm.) in 3 hr. Started 30 min. after injury 250 c.c. of dog plasma (15 Gm.) in 2 hr. Started 4½ hr. after injury	Before injury	116	125	4	41.8	1290	5.8
				15 min. after injury	110	95	15	48.3	----	6.1
				4 hr. after injury	114	145	14	48.3	1025	5.9
				7 hr. after injury	180	165	10	44.1	1130	6.0
7	7/15/41	21.6	Dog plasma, 340 c.c. (27.2 Gm.) in 4 hr. Started 30 min. after injury Bovine serum albumin, lot 17, 280 c.c. (18.5 Gm.) in 2 hr. Started 4½ hr. after injury	Before injury	146	130	8	53.7	1080	6.5
				20 min. after injury	160	140	10	59.0	---	--
				4¼ hr. after injury	180	160	10	57.2	960	6.6
				8½ hr. after injury	180	160	10	52.2	880	6.1
8	3/25/42	25.7	Crystallized bovine serum albumin CB_6, 800 c.c. (48.8 Gm.) in 8 hr. Started 15 min. after injury	Before injury	150	120	6	47.0	1415	5.6
				10 min. after injury	150	100	12	52.0	----	5.8
				2 hr. after injury	140	115	34	50.5	----	5.4
				5 hr. after injury	160	115	20	48.4	----	5.5
				8 hr. after injury	200	136	18	47.5	1175	5.6
9	3/10/42	13.6	Crystallized bovine serum albumin CB_5, 100 c.c. (30 Gm.) in 7 min. Beginning 6 min. after injury	Before injury	144	118	8	50.4	630	5.5
				30 min. after injury	136	130	7	45.6	---	7.4
				1 hr. after injury	136	120	6	45.8	---	6.2
				4 hr. after injury	160	110	6	50.0	460	5.5
10	3/17/42	18.2	Crystallized bovine serum albumin, 110 c.c. (33 Gm.) in 7 min. Started 18 min. after injury Crystallized bovine serum albumin, 80 c.c. (24 Gm.) in 5 min. Started 6 hr. after injury	After injury	110	120	18	45.7	1100	6.2
				15 min. after injury	104	100	24	46.7	----	7.3
				45 min. after injury	110	115	24	39.6	----	6.3
				2½ hr. after injury	116	124	12	46.2	----	6.6
				5¼ hr. after injury	124	124	16	51.1	1060	6.7
				8½ hr. after injury	130	120	16	42.8	940	7.7

were less impressive. In no instance was the effect of the replacement entirely comparable to that seen with continuous infusions of dog plasma. The effects of a prolonged plasma infusion are compared with albumin in Figs. 2 and 3. Note that when plasma was given there was

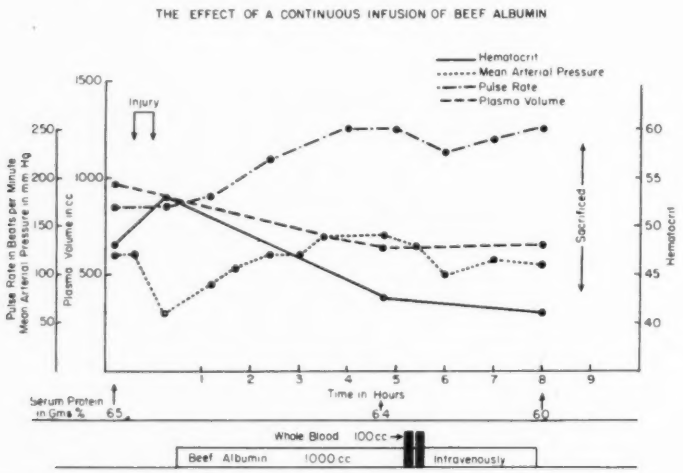

Fig. 3.—Continuous infusion of amorphous beef serum albumin prevented excessive loss of plasma and was effective in maintaining the mean arterial pressure.

little change in the pulse rate and a gradual fall in the plasma volume, no gross abnormalities were found and microscopically there was a striking amelioration of the usual late tissue changes.[4] Following continuous prolonged infusion of albumin, however, free fluid in quantities of 20 to 100 c.c. was found in the pleural and peritoneal cavities and the microscopic changes in the viscera were fairly marked although, in general, much less severe than that seen in untreated animals.

One finding which is not entirely explained was the marked reduction of the hematocrit out of all proportion to the changes in plasma volume, seen in experiment Nos. 2, 4, and 5. There was little gross loss of blood in most of these experiments, although in Nos. 2 and 5 there was quite marked oozing of blood from the wounds where vessels were exposed for sampling of blood. It is well established that saline solution infused into the blood stream in shock leaks out of the circulation not as saline but as dilute plasma.[2] It seemed possible that albumin, when given in continuous infusion, leaked out not as albumin but as dilute plasma and thereby carried with it other protein elements such as prothrombin. The possibility of an acute hypoprothrombinemia was investigated but low levels by the Quick method were found in only one, No. 2, of the five experiments, Nos. 1, 2, 3, 4, and 5, in which it was determined. Since the protein concentration remained essentialy normal, it is not likely that the decrease in hematocrit was due to changes in individual cell volume. The exact cause of the severe reduction of the hematocrit observed in these experiments is not yet explained. It is

worthy of note that similar reductions were not observed with prolonged plasma infusions.[4]

Since an infusion of amorphous albumin seemed capable of maintaining the circulation and plasma volume for short periods of time only, the possibility of using albumin as an adjunct to plasma was investigated in experiment Nos. 6 and 7. In each instance, plasma appeared to be the somewhat more effective replacement fluid (Figs. 4 and 5). However, it is quite significant that the net result in each experiment was quite comparable to that seen with plasma alone (Fig. 2). Moreover, pathologic study of the viscera of these animals disclosed the same amelioration of the pathologic changes of advanced shock that is seen following continuous infusions of plasma.

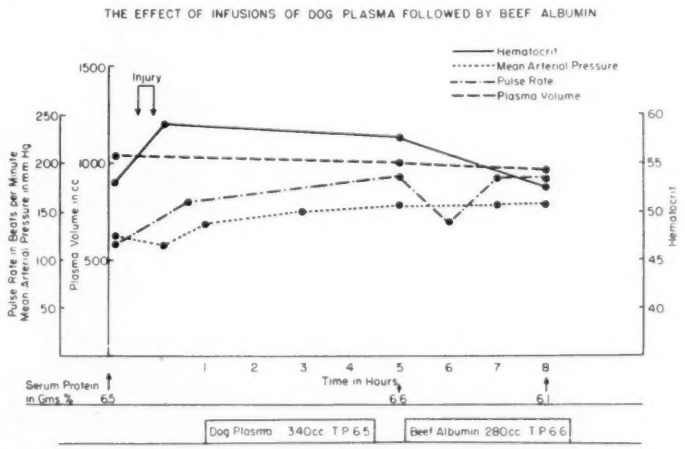

Fig. 4.—Both dog plasma and bovine serum albumin maintain plasma volume and mean arterial pressure satisfactorily.

At this point in the study, a preparation of crystallized albumin of great purity was made available to us. This was used in experiment Nos, 8, 9, and 10, in the first as a dilute solution (6 per cent concentration) and in the last two as a concentrated solution. The results of the continuous infusion of the crystallized albumin in experiment No. 8 were much more impressive than that seen following the use of amorphous albumin in experiment No. 2. However, since only one of the elements of plasma is replaced by an infusion of albumin, it is not possible to consider it a complete and adequate replacement for plasma if the losses are large and continuous. This was borne out by the fact that in the later stages of this experiment there was some oozing of blood, a rise in pulse rate, a moderate fall in plasma volume, and, on pathologic examination, moderate tissue changes especially in the kidneys, lungs, and adrenals were found.

The effects of infusions of concentrated albumin, 25 to 30 per cent, were studied in the last two experiments. The results merit considerable attention. It is evident that the plasma volume was maintained at close

to normal levels by a quantity of replacement fluid considerably less than that usually required (Fig. 6). When continuous infusions of dilute plasma or albumin are given, amounts up to 75 to 100 c.c. per hour for a 20 kg. dog are necessary to maintain the plasma volume and protein concentration. In these later two experiments, amounts of 100

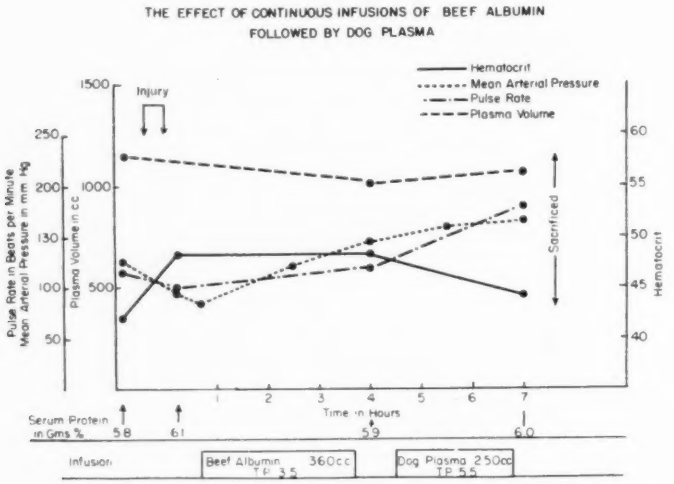

Fig. 5.—The bovine serum albumin was satisfactory in maintaining volume and pressure but not as effective as dog plasma.

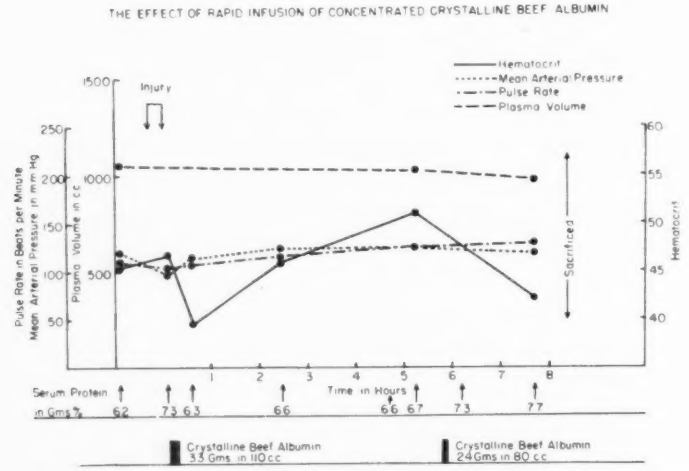

Fig. 6.—Rapid infusions of concentrated crystallized bovine serum albumin maintain plasma volume and pressure for five hours without the addition of further fluids. A second injection was as effective as the first.

and 200 c.c. seemed to accomplish the same effect for five and eight hours respectively. Whether this was accomplished by absorption of available tissue fluids into the blood stream by the concentrated protein or by the prevention of fluids being lost into the burned area is not entirely clear. There seemed to be less edema and loss of fluids into the burned area in the experiments in which the concentrated solution was

used, but no actual determination of the comparative amounts of fluid in the injured areas was attempted.

On the other hand, the pathologic changes found on post-mortem examination in experiment Nos. 9 and 10 were quite advanced for the respective duration of the experiments. The changes involved principally the lungs, kidneys, and gastrointestinal tract. The degree of congestion and edema was similar in character but not degree to that seen in untreated animals. The liver showed very little congestion but there were scattered areas of necrosis characterized by altered staining reaction of the cells and a light infiltration of polymorphonuclear leucocytes. Although these changes were fairly advanced, it is important to emphasize that there was nothing in the histologic appearance of these lesions to indicate that they were irreversible. Nevertheless, the extent of the changes is a reason for accepting the apparently excellent response of the circulation and plasma volume to therapy with concentrated plasma proteins with a certain amount of caution.

The optimum concentration of plasma or protein solutions for use in traumatic shock has not been determined. Despite enthusiastic reports[3, 11] on the use of concentrated plasma, the issue cannot be regarded as definitely settled. While it is true that in the well-hydrated individual interstitial fluid provides a large reservoir which apparently can be utilized to a great extent without danger, in the dehydrated subject or after especially severe losses, as in extensive burns, there is at least a hypothetical hazard of mobilizing extracellular fluids to a harmful degree. The excellent results of experiment No. 10, in which a concentrated solution of albumin maintained the plasma volume at close to a normal level for eight hours after an especially severe injury, indicates that the dangers are not as great as might be supposed. That there is a limit to which a concentrated solution can compensate for fluid losses is obvious and the accentuation of the visceral pathologic changes in experiment Nos. 9 and 10 suggest that the replacement was not ideal.

A determination of the optimum concentration for plasma protein when used in shock is not within the scope of this communication. It is a pressing problem which requires further study. Until further evidence is available, a reliable guide would seem to be the principle advocated by Blalock[3] of "replacing the lost fluids in the form in which they are lost" with the additional proviso that in the early stages of shock, before dehydration is established, a concentrated solution may be of value in providing an immediate excess of protein, maintaining plasma volume by utilizing available interstitial fluids, and possibly in limiting total fluid losses. The fact that concentrated plasma proteins are readily stored and transported in compact form make them extremely valuable for this purpose in the early treatment of shock in wartime.

SUMMARY

Infusions of bovine serum albumin were given to dogs after severe thermal trauma without evident toxic reaction. Continuous infusions of normal or slightly dilute solutions adequately maintained plasma volume and circulatory tone for considerable periods of time. When protein and fluid losses were large and continuous, such preparations were not quite as efficacious as plasma. When normal or slightly dilute solutions were used as an adjunct to plasma, the results were quite comparable to complete plasma replacement.

Small infusions of concentrated bovine serum albumin, 25 to 30 per cent, maintained plasma volume and circulatory tone as effectively as large infusions of normal or dilute solutions. The indications for and possible dangers of using concentrated solutions are discussed.

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VENOUS PRESSURES IN PATIENTS WITH VARICOSE VEINS*

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IN CONNECTION with a general investigation of the effects of posture on the cardiovascular system, it seemed of interest to determine the venous pressures in patients with varicosities of the saphenous veins. The frequent occurrence of varicosities in individuals whose occupations involve considerable standing has led to the belief that conditions imposed by the upright position, such as the high venous pressures in the extremities, are important factors in the development of varicosities.[1, 2] It, thus, has often been assumed that the venous pressure in incompetent, varicosed veins is abnormally high,[3] although a reasonably thorough search of the literature reveals but few studies in which the pressures have been directly measured,[1, 4-8] and only two instances[6, 8] in which parallel control determinations have been made on nonvaricosed "normal" veins. The latter study showed that when patients with varicosed veins are in the standing position, the saphenous pressures correspond closely with the hydrostatic pressure, irrespective of whether the vein is varicosed or not. We have been unable to find any reference to the levels of venous pressure in other veins of patients with saphenous varicosities.

We have studied fifty unselected patients, twenty-two males and twenty-eight females, who were referred to the vascular clinic of Charity Hospital for treatment. Twenty-five of these suffered from unilateral and twenty-five from bilateral varicosities. Four patients of the former and ten of the latter group also had hypertension (systolic pressure above 150 mm. Hg and/or diastolic pressure above 90 mm. Hg). The ages of the patients varied from 22 to 75 years, the majority being between 40 and 65 years old. Approximately two-thirds were white, the remainder colored patients. The degree and duration of their varicosities varied considerably as did their previous treatment. Some of the varices were of recent development and untreated; in other cases, the condition had been present for as long as twenty-five years and had been treated, at various times, by injections, ligations, and so forth. An additional control group of twenty individuals with no varicosities, four of whom were hypertensive, were also studied.

The general plan of the experiments was to determine the venous pressures of the saphenous veins of both extremities and of one of the

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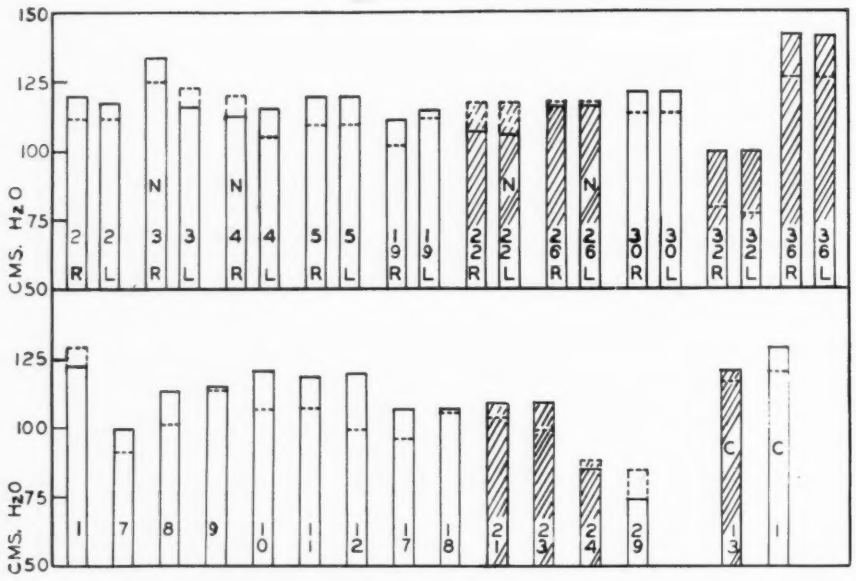

Fig. 1.—Saphenous venous pressures of patients standing. Cross-hatched bars, hypertensive patients; *N*, no involvement; *C*, control subjects, no varicosities. Hydrostatic level (distance from puncture site to fourth interspace) shown by dotted line across each bar. Numbers in each bar refer to patient's number.

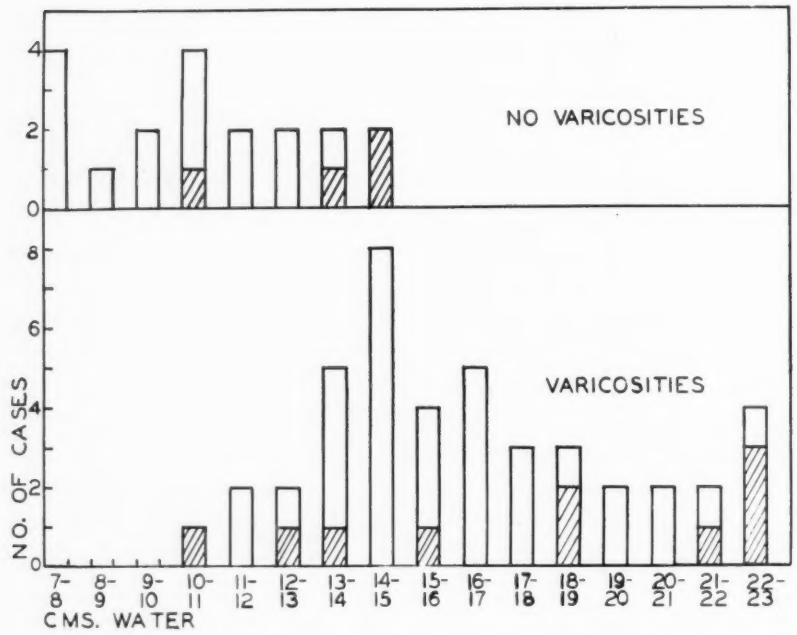

Fig. 2.—Distribution of antecubital venous pressures in recumbent patients. Cross-hatched areas indicate hypertensive cases.

antecubital veins with the patients in the standing and then in the recumbent position. The direct method of Burch and Sodeman[9] was used throughout. In the standing position, the levels of puncture depended upon the position and prominence of the varicosity. In the cases of bilateral involvement it was usually possible to determine the pressures slightly below the mid-calf region. Where the varicosities were unilateral, the punctures were made at the most accessible point of the "normal" saphenous vein and at the corresponding point of the opposite varicosed vein. Heart level was assumed to be at the fourth interspace[10] and the hydrostatic pressure was calculated as the distance between it and the site of puncture. The antecubital readings were always made with the arm at heart level. In the early experiments the measurements were made with the patient standing, then the needles were removed and the patient placed in the recumbent position on an examining table. The needles were then reinserted at approximately the same points and the measurements repeated. The relatively large number of punctures necessitated by this procedure frequently made it impractical to obtain all of the observations on the same day. The use of a tilting table in the later part of the investigation made it possible to leave all of the needles in place while the patient was passively shifted from one to the other position. This procedure also minimized muscular movements and resulted in more uniform readings. Heart level was assumed to be 10 cm. above the height of the table for the horizontal position[11] and the arm was usually placed at an angle of 45 degrees from the trunk for the antecubital determinations.

The venous pressures, as measured in the saphenous veins of patients in the quiet standing position, are shown in Fig. 1. Representative control values are also given. The results leave no question but that pressures measured under these conditions primarily reflect the hydrostatic component. The inability of many of the patients to stand quietly during the course of the observations may account for the slight variations in the hemodynamic components (pressure above hydrostatic level) as well as for the failure of the pressures to reach the hydrostatic level in seven of the experiments.[12] The use of the fourth interspace as a common reference point for heart level also introduced some error in the determinations.[12] The values which were obtained, however, are of the same order of magnitude and exhibit the same variations as do measurements of standing venous pressures of "normal" veins.[10] This is well illustrated in the cases of unilateral varicosities, where there were no significant differences between the pressures of the "normal" and the involved vein. The presence of hypertension did not seem to influence the height of the venous pressure except where some decompensation was present (Patient 32).

Fig. 2 shows the distribution of the antecubital venous pressure values in the control and varicose vein groups when the patients were placed

in the supine position. The pressures in the saphenous veins in both groups under these conditions were either the same or several centimeters higher.[13, 14] The control values were distributed in the usual fashion and ranged from 7 to 15 cm. H_2O.[15] The majority of the readings were below 11 cm., and only two patients had a pressure of over 14 cm. H_2O which is commonly regarded as the upper limit for "normal" values.[14] These two patients exhibited a hypertension and some cardiac decompensation. On the other hand, the majority of the patients in the varicose vein group had venous pressures higher than this level and their distribution curve showed a pronounced shift to the right. In many cases, the values were of the same order as found in severe cardiac decompensation, but manifestations of cardiovascular involvement were evident in only eight of the twenty cases with abnormally high venous pressure values.

Our results thus indicate that the saphenous venous pressures of patients with varicose veins are within the normal range when the individuals are in the standing position but become elevated and abnormally high when the recumbent position is assumed. Chapman and Asmussen[16] likewise found that the cardiac indices of individuals with varicose veins were within the normal range when the patients were tilted to the upright position but were considerably higher when the individuals were placed in the recumbent position. These patients also showed elevated blood volumes when they were recumbent.

These findings suggest that patients with varicosities have become adapted to higher levels of cardiovascular function which enable them to withstand the strain of the upright position without too much discomfort. When an individual shifts from the recumbent to the standing position, there is a surge of blood downward from the head, arms, and upper trunk to the subcardiac tissues. Blood which previously flowed easily and quickly back to the heart along horizontal venous channels must now climb more slowly over vertical distances of as much as a meter or more. This column of blood exerts a hydrostatic pressure almost equivalent to the force developed by the left ventricle at the peak of its systole and causes a dilatation of the veins and a local accumulation of blood. Asmussen, Christensen, and Nielsen[17] have estimated that 500 c.c. or more of blood may pool in the legs of "normal" persons standing quietly. The amount of pooling in patients with large bilateral varicosities must be considerably in excess of this amount. This loss in circulating blood volume results in a diminshed venous return and stroke output and a temporary drop in blood pressure which is partly or entirely compensated for by an increased pulse rate and a generalized vasoconstriction. The latter mechanism serves the dual purpose of preventing further flooding of the subcardiac capillary reservoirs and of shifting a large volume of blood to the dilated veins. Unless muscle tone is low, the average "normal" individual is able to

stand for relatively long periods with no cardiovascular embarrassment,[18] although it is questionable whether compensation is ever complete. The presence of large varicosities renders compensation more difficult. Chapman and Asmussen[16] found that 47 (18 per cent) of 250 patients with large varicosities complained of undue shortness of breath that was relieved in the recumbent position; 19 of these 47 also suffered mild precordial pain and palpitation, and three were women who experienced attacks of sudden dyspnea, dizziness, and precordial pain simply on standing. The patients were without gross signs of the known types of heart disease, although in some the blood pressure was slightly elevated.

While vasoconstriction probably represents an important mechanism by which blood is rapidly shifted to the dilated veins, it is improbable that this vasoconstriction is maintained over long periods of time or that the circulatory system is so regulated that any enlargement of one set of vessels is exactly balanced by an equal reduction in the size of other vessels. When, as in the development of varicosities, the vascular bed enlarges, there must be a concomitant increase in blood volume in a manner similar to that which occurs in hyperthyroidism,[19] cardiac disease,[20] and arteriovenous fistulas.[21] This increase in volume serves to fill the vascular bed, which is particularly enlarged when the patient is in the standing position, and compensates for the abnormal amount of pooling in the veins. Once the distended saphenous veins are filled, their pressures will reflect the gravity effect of the column of blood below the right side of the heart. Venous pressure will rise considerably above the hydrostatic pressure only if the intra-abdominal pressure is raised to a level which compresses the iliac vessels and vena cava and hinders the normal overflow of blood into the right heart.[8] On the other hand, when the patient assumes the recumbent position, there is less distention of the veins and the amount of blood is now greater than needed to fill the vascular bed. In other words, while compensated for the upright position, the cardiovascular system is overcompensated for the recumbent position. These patients, therefore, have high blood volumes and consequent high venous pressures when reclining.

Various explanations have been proposed for the development of varicose veins. Adams[8] believes that the erect posture has developed activity stresses which markedly increase intra-abdominal pressure and indirectly raise the saphenous pressure to abnormally high levels and that this, combined with a vulnerability in certain individuals, probably is sufficient to produce varicose veins. Irrespective of the etiologic factors which cause the stretching, the following hypothesis seems logical. Once the stretching has occurred there is a compensatory increase in blood volume in order to maintain the elastic vascular system in its usual overfilled condition and to maintain an adequate cardiac output. This results in a high pressure on the venous side of the circulation

when the patient is in the recumbent position. When the individual with varicosities assumes the standing position, there is a considerable amount of pooling in the stretched veins, and the circulating blood volume and the cardiac output diminish. Because of the initial high levels, however, the values finally achieved usually are still within the "normal" range. The venous pressure, therefore, is also at the "normal" level and reflects the gravitationally induced hydrostatic pressure.

If the above hypothesis is correct, the presence of varicosities imposes a continuous strain on the cardiovascular system, even when the patient is in the recumbent position. The heart is called upon to handle a relatively large venous return and thus do more work. The increase in blood volume may be of sufficient magnitude to induce arterial hypertension. Ligation of the veins, by removing the peripheral blood reservoirs, should have a tendency to restore "normal" hemodynamic conditions. Thus, Chapman and Amussen[16] found that the cardiac outputs and systolic pressures were definitely decreased after ligation and that there was a decided improvement in the compensation of the patients to tilting. Adams[8] found that raised intra-abdominal pressures had much less influence on the venous pressure after the veins were ligated. We have also found, in preliminary experiments, that the venous pressure may decrease and remain low after saphenous ligation.

SUMMARY

No differences were observed in the height of the venous pressure in "normal" and in varicosed saphenous veins of standing patients. In both types of veins the pressures were usually only slightly higher than the hydrostatic pressure.

The antecubital and saphenous venous pressures of patients with varicose veins were found to be significantly higher than "normal" when the patients were in the recumbent position.

These high recumbent venous pressures are believed to be due to an increase in blood volume which enables the individual to compensate for the effects of gravity while standing, but results in an overcompensated state when the recumbent position is assumed.

We are grateful to Alton Ochsner for his interest in the problem and for his permission and that of O. P. Daly to use the facilities of the vascular clinic. Thanks are also due W. D. Davis, Jr., and W. J. Trautman, Jr., for assistance in the later part of the study.

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A STUDY OF THE HEALING OF ABDOMINAL OPERATIVE WOUNDS FOLLOWING CLOSURE OF PERFORATED ULCERS OF THE STOMACH AND DUODENUM*

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THE question of the drainage of the peritoneal cavity following operation for acute perforation of a peptic ulcer of the stomach or duodenum was, until relatively recently, a hotly debated one. This was particularly true in Philadelphia in the early 1930's and it was then that this study was started. For a period of many years at the Episcopal Hospital, a definite routine for the management of perforated ulcers was strictly followed. In every case, regardless of the duration of the perforation, the operation was carried out through an upper right rectus incision with splitting of the muscle or with lateral retraction of it. The readily available fluid, especially if showing gastric contents, was evacuated and the perforation closed. During the first twenty years of this series a gastroenterostomy was added in thirty-six of the fifty cases, but in only one of the forty cases in the next four years. After establishing pelvic peritoneal drainage through a suprapubic stab wound, the operative wound was closed in layers with catgut, except for the skin, and without drainage. Thus, there was established an excellent setup for the study of wound healing in the presence of contamination, for which the surgeon had established drainage of the peritoneal cavity.

During the period between Jan. 1, 1912, and Jan. 1, 1936, ninety patients, who had been treated for their perforated ulcers as outlined above, recovered and were followed a sufficient length of time to study their wound healing. In sixty-seven, or 74.4 per cent, of these there was no evidence of infection (Fig. 1 and Table I). In only four of the wounds was there evidence of enough infection to classify them as seriously infected, and three of these were associated with disruption. In the light of recent studies about wound healing it seems likely that the disruption more probably was due to nutritional disturbances than to infection, but there is insufficient data in these cases to reach such a conclusion.

The factors available for study in this series were the duration of the perforation, the quantity of the peritoneal fluid and the characteristics

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of the fluid. Unfortunately, three other important factors could not be studied because of lack of sufficient information to make them of statistical value. These other factors are the bacteriology of the peritoneal fluid, the time interval between the last intake of food and the perforation, and the size of the perforation.

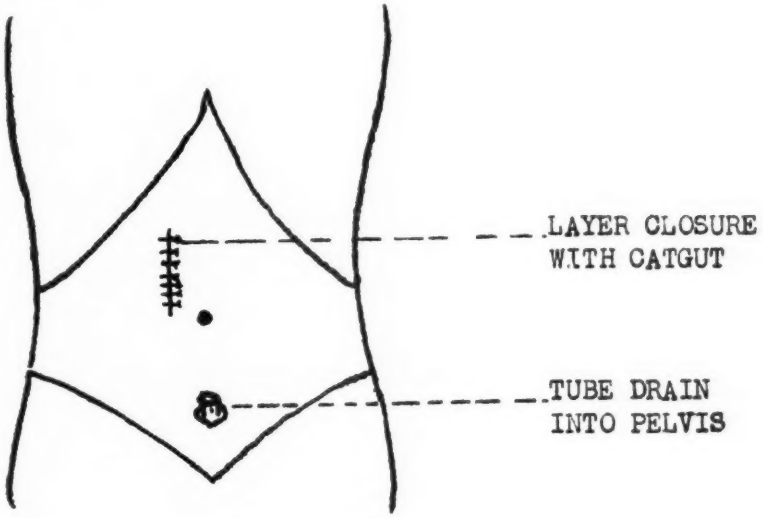

Fig. 1.

The relationship between the duration of the perforation and the character of the wound healing was not consistent. Of those perforations closed within six hours of their occurrence, 79 per cent healed without evidence of infection, and yet, in those operated upon between twelve and eighteen hours after perforation, 83 per cent healed without evidence of infection (Table II).

When the amount of fluid found at operation is considered, there is seen to be some apparent correlation between the amount of fluid and the healing of the operative wound. The less the amount of fluid the better the chance for the wound to heal without evidence of infection (Table III).

Between the character of the fluid and the healing of the wound there also seems to be a definite relationship. Clear fluid was associated with primary wound healing in 82 per cent of the 51 cases. When gastric

TABLE I

WOUND HEALING*

Primary	67 or	74.4%
Infected	23 or	25.6%
Total number	90	100 %

*Acute free perforations of gastric and duodenal ulcers, Episcopal Hospital, Jan. 1, 1912, to Jan. 1, 1936, surviving patients having primary closure of operative wound combined with suprapubic drainage of pelvis.

TABLE II

DURATION OF PERFORATION IN RELATION TO WOUND HEALING INFECTION

DURATION	NONE	SLIGHT	MODERATE	SEVERE
Less than 6 hr. (38)	30 (79%)	1	6	1 (Disruption)
6 to 12 hr. (39)	27 (69%)	6	4	2 (1 Disruption)
12 to 18 hr. (6)	5 (83%)	1	0	0
18 to 24 hr. (4)	2 (50%)	0	1	1 (Disruption)
24 to 48 hr. (3)	3 (100%)	0	0	0

TABLE III

RELATIONSHIP BETWEEN AMOUNT OF FLUID AND WOUND HEALING

AMOUNT OF FREE FLUID	DEGREE OF INFECTION OF WOUND			
	NONE	SLIGHT	MODERATE	SEVERE
None (6)	6 (100 %)	0	0	0
Small (28)	23 (85.7%)	1	4	0
Moderate (36)	25 (69.4%)	5	4	2 (Disruptions)
Large (20)	13 (65 %)	2	3	2 (1 Disruption)

TABLE IV

RELATIONSHIP BETWEEN CHARACTER OF FLUID AND WOUND HEALING

CHARACTER OF FLUID	DEGREE OF INFECTION OF WOUND			
	NONE	SLIGHT	MODERATE	SEVERE
Clear or not specified (51)	42 (82.3%)	1	7	1 (Disruption)
Gastric contents (19)	12 (63.1%)	3	3	1 (Disruption)
Pus (14)	7 (50 %)	4	1	2 (1 Disruption)

contents were noted in the fluid, 63 per cent of the wounds healed without evidence of infection, and when there was frank pus, only one-half of the wounds healed by primary intention (Table IV).

The operative wounds in these cases were not washed out before closure, nor were the wound edges protected in any way from the contaminating fluid. Layer closure was done with No. 1 or 2 catgut for everything except the skin, which was closed with metal clips or non-absorbable sutures. No antiseptics were used and this was before the sulfonamide era. Notwithstanding, it has been shown that the large majority of these soft tissue wounds healed without evidence of infection. As it has been repeatedly demonstrated that the soft tissues are less resistant to infection than the peritoneum, it would seem reasonable to conclude that in this series of cases peritoneal drainage was rarely, if ever, needed. Furthermore, it seems that even the soft tissue

wounds do not become infected if the perforation can be closed before there has been any great leakage of gastric or duodenal contents or accumulation of much peritoneal fluid. Now, with the addition of the sulfonamide drugs, it would seem that one should hesitate to establish peritoneal drainage unless the perforation cannot be closed adequately or there is a localized collection of pus.

As a matter of giving the background for this series of ninety cases, certain other data should be presented. During the twenty-four years in which these cases occurred there were 730 patients with ulcer of the stomach and duodenum admitted to the Episcopal Hospital, 232 of whom had acute perforations. During the first twenty years 164 patients were admitted and 57, or 34.75 per cent, of them died. In the next four years 68 were admitted and 13 of these died, giving a mortality rate of 19.11 per cent. During the entire period of twenty-four years only 13 patients were operated upon without establishing peritoneal drainage. Only one of these died, and that was due to pneumonia developing after a secondary operation for the establishment of peritoneal drainage in a patient whose abdomen had been closed without drainage and whose peritoneum showed no evidence of inflammation at the second operation. Four of the wounds showed some evidence of infection, but in no case was there a suggestion of peritoneal involvement.

SUMMARY

1. At the Episcopal Hospital in Philadelphia, between 1912 and 1936, acute perforations of gastric and duodenal ulcers were treated by closure of the perforation with or without gastroenterostomy. The operative wound was closed in layers with catgut after establishing suprapubic peritoneal drainage.

2. Ninety of these patients recovered and were followed sufficiently long to observe the nature of their wound healing.

3. Sixty-seven, or 74.4 per cent, of the wounds healed by primary intention. Twenty-three, or 25.6 per cent, of the wounds showed some evidence of infection.

4. There was no apparent correlation between the duration of the perforation and the wound healing. Of those under six hours, 79 per cent healed without infection, whereas 83 per cent of those between twelve and eighteen hours healed without evidence of infection.

5. There seemed to be some correlation between the amount of fluid and the nature of the wound healing. Of the six cases in which there was no fluid, all of the wounds healed by primary intention. In twenty-eight with small amounts of fluid 85 per cent healed without infection. Of thirty-six with moderate amounts of fluid, 69.44 per cent healed without infection. Of twenty with large amounts of fluid, 65 per cent healed without evidence of infection.

6. The character of the fluid appeared to be related to the wound healing. In fifty-one cases the fluid was clear, and 82.3 per cent of these wounds healed by primary intention. In nineteen cases gastric contents were seen in the peritoneal fluid. Of these wounds, 63.15 per cent healed without evidence of infection. In fourteen cases in which there was frank pus, 50 per cent of the wounds healed by primary intention.

CONCLUSIONS

The healing of the contaminated, undrained operative wounds in these ninety cases of acute perforations of gastric and duodenal ulcers indicates that in this group of cases peritoneal drainage was rarely, if ever, needed. It should then follow that peritoneal drainage is not needed in any case when the perforation can be satisfactorily closed and there is no walled off pus. With the addition of sulfonamide therapy this conclusion seems justified.

SULFATHIAZOLE IN CHRONIC OSTEOMYELITIS

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THE introduction of chemotherapy has been a far-reaching advance in the treatment of osteomyelitis. Much of the chronic suffering caused by this disease can be relieved with the help of the sulfonamides. In the past the therapy of osteomyelitis has been a sorrowful succession of "cures" which did not materialize as was hoped. One method after another became popular and then fell into disrepute. The surgeon demonstrated his dissatisfaction by trying one mode of therapy after another.

At one period acute osteomyelitis was considered a surgical emergency, and the cortex of the bone was drilled in search of pus, even before the roentgenologic changes had made themselves manifest. In the later stages of the disease, meticulous saucerization and sequestrectomy were carried out with great care and completeness, but even so, chronic suppuration with sinuses continued, often for years. Various bactericidal agents have been used. Dakin's solution was used widely in World War I. Then bacteriophage became popular and later there was a revival of the maggot treatment. Most surgeons agree that a definite step forward was made in the adoption of the Orr treatment (postoperative plaster immobilization of the lesion, including the joint above and below, and infrequent changes of plaster for dressings). As a rule, the wounds so treated were cleaner and healed more rapidly than those which were frequently dressed.

Modern chemotherapy was applied early to the problems of bone infection. Dickson, and associates,[1] Dively and Harrington,[2] Hoyt and associates,[3] and Key and associates[4] have been especially interested in the effect of the sulfonamides on bone infections.

This series of cases is presented with the belief that our experiences at the Lahey Clinic with chemotherapy in bone infection will aid in the clarification of present treatment. The majority of our patients have had either old chronic osteomyelitis with sinus formation, or an acute reactivation of previous osteomyelitis, flaring up after a quiescent period of a number of years.

TREATMENT

The general plan of treatment, a combination of several forms, may be divided into three stages:

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1. *Preoperative.*—The patient with osteomyelitis has at least one week of bed rest in the hospital before operation. During this period a course of sulfathiazole is given, the routine dose being 15 gr. every four hours or 90 gr. in a twenty-four-hour period. The blood level of the drug, red and white blood counts, and urinalysis are determined at frequent intervals. Sulfathiazole blood levels of 3.5 to 11 mg. are reached, the more usual levels being in the lower brackets. When sulfathiazole has to be discontinued because of a reaction, the chemotherapy is continued with sulfadiazine, after the reaction has subsided. Sulfadiazine is less toxic and higher blood levels are easy to maintain. We have had insufficient experience with sulfadiazine to compare its efficacy in staphylococcal osteomyelitis with that of sulfathiazole. It is our present plan to change to sulfadiazine in any case in which we have difficulty with sulfathiazole.

After a week of preparation, the patient is ready for surgery. Usually there has been a diminution of pain, heat, swelling, tenderness, fever, leucocytosis, and sedimentation rate, due, I believe, to the combined effects of sulfatherapy and rest. In one instance (Case 2), the patient had such dramatic relief that he insisted on going home without operation. However, three weeks later the osteomyelitis again became acute, and operation was performed after another week of chemotherapy.

2. *Operative.*—The routine procedure is a wide, careful saucerization of the infected area of bone. If a sinus tract is present, before making the incision methylene blue is injected into it to aid in the dissection of the sinus tract and to help in locating the entrance of the tract into the bone. If more complete study of the sinus tract is indicated in planning the operation, lipiodol is injected and roentgenograms are taken preoperatively.

In these operations a tourniquet is used as a regular course, without evidence of spreading the infection. The dry field which a tourniquet provides is of the greatest aid in the removal of diseased soft tissue as well as bone. The extremity is first elevated, then an Esmarch rubber bandage is applied tightly from the toes or fingers in a spiral, upward; then the tourniquet, which consists of a flat rubber band around the upper thigh and a blood pressure cuff on the upper arm, is applied.

An elliptical incision is made about a previous operative scar or sinus, if present. The dissection is carried down to the bone removing the infected scar, granulation tissue, and sinus tract, brightly stained with methylene blue. As much of the scar tissue as possible is excised, bearing in mind the necessity for adequate closure of the wound by covering the bone with soft tissue. The cavity in the bone is opened freely with gouge and chisel, wherever possible creating outwardly sloping walls with no overhang or re-entrant angles. A motor burr may be helpful in thus saucerizing the bone. Sequestra, if present, are removed. The wound is washed carefully with saline solution to remove all bone particles and before closure the tourniquet is removed and hemostasis

established. Sulfathiazole powder is then placed in the wound. We have used 5 to 15 Gm. (75 to 225 gr.), depending on the condition and size of the wound. Primary closure is then effected without a drain and after each layer is closed, additional powder is dusted into the wound. For a time sulfathiazole sodium was used in preference to sulfathiazole, because it was more soluble. Then the use of sulfathiazole sodium was discontinued because of its high alkalinity, although we had no difficulties which we could ascribe to it. The deep layers of the wound are closed with catgut and the skin with silk, all interrupted sutures. A dry dressing and a circular plaster cast extended to immobilize the joint above and below the involved bone are applied. For example, in femoral osteomyelitis a single hip spica bandage is applied, while for osteomyelitis of the tibia, the knee and ankle joints are immobilized.

3. *Postoperative.*—The sulfathiazole routine is kept up for at least two weeks unless some contraindication develops. The plaster is not removed, nor is the wound inspected.

Two weeks after operation the plaster is changed and the wound sutures are removed. We are guided in the length of time the plaster is left on by the appearance of the wound. This period varies from four to eight weeks, and weight bearing is begun in lower extremity cases in from four to eight weeks after operation. Postoperative sulfathiazole administration has not been kept up longer than six weeks even when the wound has persisted in discharging.

REPORT OF CASES

The major details of treatment and results are recorded herewith in all cases of osteomyelitis treated at the Lahey Clinic from January, 1941, to June, 1942.

CASE 1.—A 25-year-old man had had osteomyelitis of the right femur which was drained surgically ten years before. For the last three years he had had an actively draining sinus in the old incision with increasing pain. Sulfathiazole was started only twenty-four hours before operation and was continued to five days after operation, at which time it was discontinued because of nausea. The average sulfathiazole blood level was 3.6 mg. The sinus, which was found to lead into a large cavity behind the femoral shaft, was excised. No aperture into the marrow cavity was found, and the bone was not saucerized. Fifteen grams of sulfathiazole sodium plus 5 Gm. of sulfathiazole were placed in the wound, which was closed primarily, and a circular plaster cast from the toes to the groin was applied. Nonhemolytic *Staphylococcus albus* was cultured from the abscess cavity. In five weeks the wound was completely healed and dry. At thirteen months after operation the wound had remained healed, dry, and painless and there was no roentgenologic evidence of activity.

Comment.—Primary closure occurred, with rapid healing of a large, soft tissue abscess which had drained for three years. The good result, in spite of the short course of sulfathiazole, was probably due to the absence of bone involvement.

CASE 2.—A 25-year-old man had had osteomyelitis of the right femur and suppurative arthritis of the right hip at the age of 3 years. At the age of 19 years a flare-up of the osteomyelitis with drainage occurred, and two weeks before admission to the clinic there was a sudden reactivation with pain, heat, tenderness, swelling, fever, and a sedimentation rate of 70. On admission there was no fluctuation and the roentgenograms showed no cavitation or sequestration. For twenty days he was treated with bed rest and 90 gr. of sulfathiazole daily. After the first eleven days an abscess localized in the right groin and was incised and drained. The cavity was of such shape that it could not be closed primarily. Five grams of sulfathiazole were placed in the wound and the superficial portion was packed. The abscess cultured *Staph. aureus*. The average sulfathiazole blood level was 4.2 mg. and the patient tolerated the drug well. Since the hip had become ankylosed years before, a cast was not applied. The abscess healed in five weeks, and has remained so after nine months.

Comment.—This patient had an adequate course of chemotherapy and did well.

CASE 3.—A 36-year-old man had had an operation performed five years previously for acute osteomyelitis of the right tibia. Five months previously he began to have pain at the former site of bone infection. On admission, pain, redness, swelling, and tenderness were present over the upper tibia, and roentgenograms revealed two large cavities in the upper tibia (Fig. 1). He received 90 gr. of sulfathiazole daily for twelve days, maintaining an average blood level of 3.5 mg. The pain, redness, swelling, and tenderness were relieved and he left the hospital against advice.

He returned three weeks later because the process again had become acute. After nine days more of oral sulfathiazole, saucerization was carried out and two connecting abscess cavities filled with thick pus were found in the upper tibia. These cultured *Staph. aureus*. Five grams of sulfathiazole sodium were placed in the wound, which was closed without drainage, and the leg was placed in a circular cast from toes to groin. After operation he received 60 gr. of sulfathiazole daily for five weeks, with an average blood level of 6.7 mg. At discharge, five weeks after operation, the cast was removed; the wound had remained healed and weight-bearing was begun. At six months after operation he is free from symptoms and the wound is healed.

Comment.—A good result was obtained in spite of extensive bone involvement. He had adequate sulfonamide therapy. A course of sulfathiazole without surgery failed.

CASE 4.—A 25-year-old man had been operated upon elsewhere ten years previously for acute osteomyelitis in the right lower tibia. For the last seven months he had had pain in the lower tibia of increasing severity with swelling and tenderness, so that he became unable to work. Roentgenologic examination of the ankle showed a cavity, 12 cm. in length, in the lower tibia, extending nearly to the joint (Fig. 2). Sixty grains of sulfathiazole were given daily for four days, and then saucerization and primary closure were carried out (Fig. 3). At operation 5 Gm. of sulfathiazole were placed in the wound, which cultured *Staph. aureus*. A long leg cast was applied from toes to groin. Because of nausea and progressive anemia, the sulfathiazole had to be stopped eight days after operation, though the average blood level was 2.7 mg. Two weeks postoperatively there was slight discharge from the wound. Six weeks postoperatively, when the plaster was left off, the wound was healed, and one year later there was no pain or evidence of activity.

Comment.—A good result was obtained in a patient with a large bone abscess though he had a rather small amount of chemotherapy after operation.

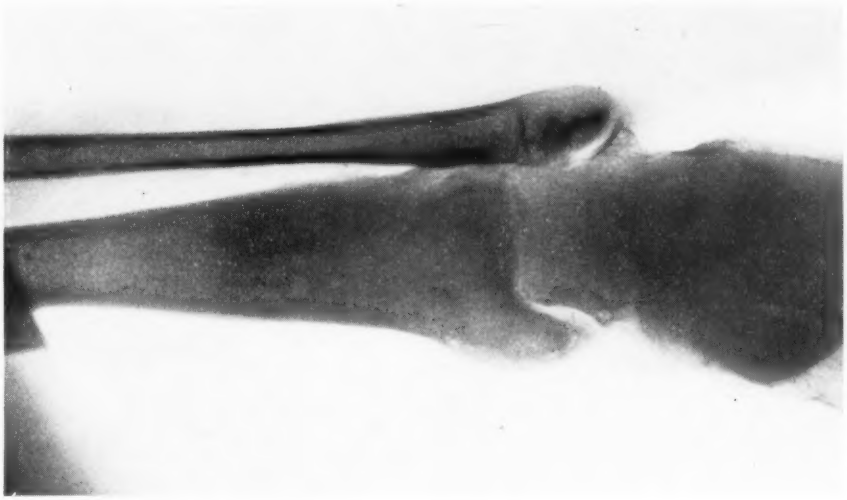

Fig. 2.—Before operation, showing osteomyelitis of the lower tibia. Extensive pus-filled cavity present.

Fig. 1.—Osteomyelitis of the upper tibia treated by saucerization, sulfathiazole orally and locally, primary closure, and plaster immobilization.

CASE 5.—A 15-year-old schoolboy entered the hospital because of pain and swelling just above the left wrist of two months' duration. Roentgenograms were consistent with either a Brodie's abscess with marked bone thickening or with a Ewing's endothelioma involving the lower radial shaft (Fig. 4). Because of the possibility of malignancy, a biopsy specimen was taken, and "chronic inflammation" was the pathologic finding. Therefore, saucerization was done, and 5 Gm. of sulfathiazole were placed in the wound. No oral chemotherapy was given either before or

Fig. 3.—Treatment consisting of saucerization, sulfathiazole, primary closure, and plaster immobilization resulted in healing.

A. *B.*

Fig. 4.—*A*, Sclerosing osteitis of radius. Saucerization alone without chemotherapy resulted in a recurrence of activity. *B*, Second procedure: saucerization with oral and local sulfathiazole was successful.

after operation. The final microscopic sections were consistent with osteomyelitis. A culture showed no growth.

Five months after the first saucerization a second operation became necessary, as pain, swelling, tenderness, and heat had returned soon after the first procedure. Ninety grains of sulfathiazole were given for three days before operation and for eight days afterward, the average blood level being 4 mg. During operation 5 gr. of sulfathiazole were implanted. Thereafter the pain subsided and four months later he was free of symptoms.

Comment.—This Brodie's abscess of the radius with extensive sclerosis failed to yield to saucerization and local chemotherapy. A second operation with preoperative and postoperative chemotherapy was successful.

CASE 6.—A 35-year-old man had had acute osteomyelitis of the left lower femur twenty-four years before admission. For the last seventeen years he had had an actively draining sinus which led from a large cavity in the lower femoral shaft to a large, depressed, old incisional scar with turned-in edges. Sulfathiazole was begun, 60 gr. a day for the first two days and then 90 gr. a day for four more days, at the end of which time the blood level was 5.8 mg. Saucerization and primary closure were performed, leaving 15 Gm. of sulfathiazole sodium in the wound, and applying a cast from toes to groin. The next day he had a sulfathiazole reaction with large, red, raised blotches on the skin. Several days later when the drug was begun again the reaction reappeared, so he received virtually no postoperative sulfathiazole therapy. The reaction increased about the wound, and three sinuses developed though the leg was kept in plaster for four months.

Because of the persisting sinuses he was hospitalized six months later, and another attempt was made to give sulfathiazole. The second day his temperature rose to 103° F., and the drug was discontinued. The next day he had a convulsive seizure. No definite cause for this was found, and it was possibly a drug reaction. However, sulfadiazine was tried without incident. He received 90 gr. daily for ten days before operation and for three weeks afterward, with an average blood level of 6.5 mg. At operation the sinus tracts were excised, and a thin sequestrum 1.5 inches long was removed. Five grams of sulfathiazole were placed in the wound, and primary closure was tried again. At three months after operation a small sinus persisted in the wound.

Comment.—Attempted primary closure in osteomyelitis of the femur with a chronic sinus failed. The patient could not tolerate sulfathiazole, and this is the probable cause of failure. It is too early to evaluate the result of the second procedure with a course of sulfadiazine, but it was more successful than the first procedure, at which time chemotherapy could not be used.

CASE 7.—A 44-year-old man had had osteomyelitis of the left lower femur with a draining sinus ever since the primary operation in 1917, twenty-four years before. He was given 60 gr. of sulfathiazole a day for one week preoperatively and for two weeks postoperatively. The sinuses, one medial and one lateral over the lower femur, were injected with methylene blue and were dissected out. No bone focus was found. A culture showed beta-hemolytic streptococcus, hemolytic and nonhemolytic *Staph. aureus* and *Staph. albus*. Five grains of sulfathiazole were placed in the wounds. A primary suture was done, and a cast applied from toes to groin. The average sulfathiazole blood level was 4.2 mg. The wounds healed uneventfully, and at six months after operation he was free of symptoms.

Comment.—There was successful primary closure of a sinus following osteomyelitis of the femur which had drained for twenty-four years. The patient tolerated sulfathiazole well.

CASE 8.—A 29-year-old man entered the hospital desperately ill, toxic, dehydrated, severely anemic, and in great pain with an acute osteomyelitis involving the entire right femur, except for the upper fourth. He was treated with five transfusions, fluids, a hip spica, and sulfathiazole. His general condition rapidly improved, he became comfortable, and began to gain weight. In his hospital stay of ninety-five days he was given sulfathiazole on sixty days with no untoward effects except for several temperature elevations which were thought to be due to the drug. There was no abscess formation, and no incisions were made. Diagnostic aspiration cultured *Staph. aureus.*

Comment.—It is too early to know the end results in this case, but the acute process subsided without any surgical procedure.

CASE 9.—A 41-year-old man entered the hospital with pain in the right knee region of eight weeks' duration. There was no previous history of osteomyelitis. Roentgenograms showed an area of dense sclerosis in the lower femoral shaft, consistent with a sclerosing osteitis of Garré. However, at operation a bone abscess cavity, centrally located, was found and saucerized. Eight grams of sulfathiazole were placed in the wound which was closed by primary suture, and a cast was applied from the toes to the groin. The culture from the abscess was *Staph. aureus.* The patient then received 90 gr. of sulfathiazole a day for eighteen days, which produced an average blood level of 5.6 mg., and also an anemia which required two transfusions. Eighteen days after operation, slight drainage occurred, and he was discharged walking with crutches.

Eight months after the first operation he was readmitted and the persistent sinus tract was excised. Sulfathiazole was placed in the wound, which was subsequently closed and has remained so for the last fifteen months.

Comment.—A bone abscess of the femur was treated in a routine manner. A second operation on the persisting sinus resulted in healing. The patient tolerated sulfathiazole well.

CASE 10.—A 41-year-old man had had acute recurrent osteomyelitis of the lower right femur for the last twenty-two years. Pain, heat, swelling, and tenderness had been present over the right lower femur for the last six months. Ninety grains of sulfadiazine were given daily for eight days before operation and for eighteen days afterward, maintaining an average blood level of 8 mg. without reaction. Saucerization was carried out and an extensive cystic area containing pus was found. Five grams of sulfathiazole were placed in the wound before primary closure. The cast was left on for five weeks after operation, at which time there was still slight drainage from the wound. The culture at operation showed *Staph. aureus.* At eight weeks after operation sinus drainage was still present, but we have been unable to follow this case.

Comment.—Saucerization was carried out on an extensive, old, femoral osteomyelitis with sinuses persisting at eight weeks. The delayed healing may be due to the fact that sulfadiazine was used.

CASE 11.—A 30-year-old woman entered the hospital with a third flare-up of osteomyelitis of the left lower tibia, acutely painful for three days. The original on-

set of the osteomyelitis was twenty-three years before. The roentgenograms showed bone thickening with a central area of rarefaction in the lower tibial shaft. There was a large, wide, depressed scar over the tibia with poor quality skin adherent to the bone. At operation the old scar was excised and the tibia saucerized. To effect primary closure a relaxing incision was made medially. Five grams of sulfathiazole were placed in the tibial wound, and a long leg plaster was applied. Three days after operation the sulfathiazole was stopped because of nausea. Three weeks later the operative wound was not healed and was resutured; the defect left by the relaxing incision was grafted. Ninety grains of sulfadiazine were given for eleven days, with an average blood level of 7 mg. The wound healed in two weeks, and had remained so when last seen six months later.

Comment.—The good result clinically was due in part to sulfadiazine by mouth rather than sulfathiazole, which the patient could not tolerate.

CASE 12.—A 26-year-old man had had a right femoral osteomyelitis which had been increasingly painful for the last six months. The original attack occurred fourteen years before. Roentgenograms showed bone thickening, irregularity, and a large cystic area in the shaft. Before operation was undertaken, sulfathiazole, sulfadiazine, and sulfanilamide were tried successively, but he was sensitive to them all. At operation the wound was saucerized and packed with vaseline gauze. Ten grams of sulfathiazole were placed in the depths of the wound. A spica bandage was applied. Three months later the wound was closing gradually.

Comment.—This case shows the difficulties of treatment when sulfatherapy cannot be used.

CASE 13.—A 26-year-old man had been having progressive pain and tenderness above the left lower femoral region for the last six months. The original attack occurred twelve years before, and three drainages were done within two years. Exploration was performed before we began using oral chemotherapy, but 40 gr. of sulfanilamide were placed in the wound which cultured hemolytic *Staph. aureus.* A vaseline pack was left in the wound, and despite this healing was conspicuously rapid, requiring but three weeks. Three years later the wound had remained healed, the patient was free of symptoms.

Comment.—The healing was rapid without oral chemotherapy, probably because we were dealing with a soft tissue abscess rather than a bone focus.

SUMMARY

1. Thirteen cases are presented to demonstrate the details of treatment of osteomyelitis with chemotherapy. Healing took place promptly in ten of the thirteen cases, and in two of the three remaining cases chemotherapy could not be given because of reaction to the drug.

2. The recommended treatment of chronic osteomyelitis consists of:

a. A course of chemotherapy and bed rest in the hospital for one week before operation. Ninety grains of sulfathiazole are given in twenty-four hours.

b. The operative procedure consists of saucerization; local sulfathiazole in the wound, 2 to 15 Gm., according to the size of the wound;

primary closure without drainage, all wound levels being dusted with sulfathiazole; and plaster immobilization, including the joint above and below the site of the lesion.

c. Postoperative chemotherapy with oral sulfathiazole for a period of at least two weeks.

3. In seven cases saucerization was done. Five healed promptly, and two did not. Both refractory cases were sensitive to sulfathiazole.

4. In five other patients saucerization was not done because of actively draining sinuses without gross evidence of bone infection. All these healed promptly with primary closure.

5. If patients cannot tolerate sulfathiazole we have tried sulfadiazine, though we have had insufficient experience with it to report on its use.

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SOLITARY ECCENTRIC (CORTICAL) ABSCESS IN BONE

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THE apparently occult nature of solitary eccentric (cortical) abscess in bone as seen clinically and the lack of complete agreement between our experiences and those of others have prompted a review of the records of all cases in which patients suffering from cortical abscess of bone were seen at the Mayo Clinic over a period of ten years, including 1941. Besides the cases of cortical abscess on which data are given here, we reviewed the records of the cases of tuberculosis of long bones, osteitis of Garré,[1] acute and chronic osteomyelitis, Brodie's abscess,[2] osteoma, and osteochondroma. This was done for the reason that confusion with those categories not only is possible, but does occur. Limitation to single lesions was self-imposed and not because they are believed to occur only in this manner. They were seen with other lesions concomitantly, as chronic osteomyelitis.

We are concerned with single, uncomplicated lesions, which give rise to a rather definite syndrome, pursue a regular benign course, and are susceptible to complete surgical eradication. They occur in both the long and the short bones, being characteristically placed, lying within, subjacent to, or superposed on, the cortex, occasionally in the neighborhood of an articulating surface. The exciting center of the lesion itself is minute, not exceeding a few millimeters in diameter as seen both at operation and in the roentgenogram. It elicits a variable mass of reaction, dependent seemingly upon the location with respect to the cortex and little affected by the age of the lesion.

STATISTICAL STUDY

Twenty-four patients were found to fall in this group. Their ages varied from 3 to 55 years. Twenty-one of the total were distributed nearly equally among the first three decades of life, the variation not being significant. Six were from 1 to 10 years of age, eight were from 11 to 20, and seven were from 21 to 30. The remaining three were in the fourth and fifth decades. There were ten female and fourteen male patients. Fifteen abscesses were found on the right of the body and nine on the left.

Brodie's abscess was encountered twenty-six times in the same period, while the osteitis of Garré was found but five times. There were twenty-

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nine cases of periostitis definitely not in this group. Other possibly confusing diseases, such as osteitis, occurred ninety-six times including syphilitic osteitis. The tibia and the femur were the most common sites, accounting for twenty of the patients in this group. The lesion was seen also in the fibula, the radius, the os calcis, and the patella. There was no apparent predilection with respect to the site, as from proximal to distal portions of the long bones, three occurring in each of the thirds of the femur, and four in each of the superior and middle thirds of the tibia, while there were three in the lower third of that bone.

CLINICAL PICTURE

The clinical picture is of a relatively mild but troublesome condition. Pain is observed constantly, being rarely excruciating but often aching. There is a strong tendency to wax and wane. Exacerbations occurred commonly in changes of weather or when the patient stood for a long time or subjected himself to other unusual exertion.

The patient's localization of the pain is accurate to a high degree in most instances, the exceptions being in those cases in which the lesion is in the upper regions of the femur. In these cases complaint was made of pain about the lower or lateral part of the thigh or the knee, as is fairly common in other lesions about that region. Pain occurred at night and, when it did, was sharp, particularly among children, who cried out and awakened. Nocturnal pain was also more common as the disease process became older.

Swelling was the next most common symptom, occurring in seventeen of the twenty-four cases. This was more in the nature of a thickening and induration and, when marked, was accompanied by redness and increased heat. Swelling is most common in the lesions of the middle third of the tibia. Atrophy or swelling may occur in lesions of the superior regions of the femur, those about the neck chiefly giving atrophy.

A limp was present in cases of affections about the joints, as in the neck or the lower part of the femur and in the superior thirds of the tibia, and, in a few instances, in other bones, particularly in the os calcis and the patella. The apparent age of the lesion seems to have little to do with the limp, being present in one case for nine years, and in another for but two months.

The chronicity of the complaint is striking. One patient had had pain for thirty-five years, another for twenty-seven years, and a third and fourth for ten and nine years. On the other hand, one who had bumped his arm two months prior to examination noted continuous enlargement for that period. All of these displayed typical findings. Eleven of the twenty-four patients had complained for a period of one year or less; nine of these were seen before six months. Eight had complained for from one to six years, the remaining five from that time to thirty-five years.

The physical findings are not remarkable. Thickening and induration to palpation in those regions that were accessible were found in most instances. Limping was found in those in which there were lesions near a joint. Redness over the site of the induration was noted rarely. Jarring of the involved bone brought on increased pain only

Fig. 1.—Right tibia of white boy, aged 13 years, who complained of occasional limping, which had been present for nine years. Four months prior to examination aching began in lower part of right leg. Pain was present night and day, or when at rest. A small bone in the right foot had been fractured eleven years previously. There were 1 inch (2.5 cm.) atrophy of right thigh and 1½ inches (4 cm.) atrophy of right calf. There was pain on pressure over the right tibia.

inconstantly. Fever was found in only one case; the oral temperature was 99.6° F.

ROENTGENOGRAPHIC FINDINGS

The roentgenologic examination was the greatest aid, the picture being definite. The minute exciting lesion is characteristically seen, radiolucent, located within or beneath the cortex, but most commonly in the

Fig. 2.—Left femur of white girl, aged 13 years, who had complained of pain in the left thigh and knee for three months. She had lost five pounds (2.3 kg.) in the past two months. Pain was chiefly at night. Swelling was present. There was no tenderness or fever.

osteoplastic reactive portion of the periosteum (Fig. 1). Here a word may be said about the interpretation of the roentgenogram. The appearance of the dark central portion as in Fig. 2 apparently locates it as lying in the cortex, while in Fig. 3 it is apparently superposed on the cortex. It must be evident that the projection of the shadows may account for the variation of the appearance to a certain extent. How-

Fig. 3.—Right femur of white woman, aged 55 years, who complained of pain and swelling in the right thigh. Thickening about the right thigh was palpable and the right thigh was slightly tender. The patient had had tonsillitis two years previously. She had injured the right thigh twenty-seven years before she was seen. The injury had necessitated rest in bed for one and one-half months. This was followed by limping for three months.

ever, we agree with others that the lesions do occur within and on either side of the cortex. Reaction with the osteosclerosis occurs about the lesions uniformly and is the pathognomonic portion of the picture,

Fig. 4.—Right tibia of white man, aged 23 years, who complained of aching at night, which was relieved by heat. There was never any limp. There was a swelling on the lateral aspect of the tibia 3 inches (8 cm.) superior to the malleolus but no tenderness or reddening. The motion of joints was normal. A year before, the patient had struck the leg against a cement step. No bruising occurred.

especially its eccentric position. Relatively enormous elevation of the periosteum is seen with heavy densification. Medullary reaction is present also, as seen in Figs. 1, 2, 3, 4, and 5. Very little medullary

disturbance seems present in every instance. Fig. 6 represents an unusual patellar lesion.

As one would expect, the organization is dependent on the time the lesion has been present. For instance, note Fig. 2 in comparison with

Fig. 5.—Left femur of white girl, aged 7 years, who had complained of limping for four months. There was pain in the left knee. The patient had an oral temperature of 99.5° F. after one month in bed. There was limitation of motion at the hip and slight spasm of the psoas muscles but no definite tenderness. Brucella agglutination was negative. The sedimentation rate was 20. The patient was given sulfathiazole, and fever abated after one month.

Fig. 3. In the latter, the lesion has been present for twenty-seven years and has undergone extensive organization, complete with the formation of an apparently secondary cortex, and with more or less restoration of the original cortex.

Fig. 6.—Right patella of white woman, aged 27 years, who complained of pain and "popping and crackling" in knee, present for ten years. Tonsillitis was graded 2. There was some thickening to palpation about the anterior portion of the knee.

In Fig. 4, an interesting problem is offered in diagnosis, not only from the roentgenologic standpoint, but from the clinical viewpoint as a whole. A question immediately arises as to the presence of a

Ewing tumor. The visibility, however, of the minute radiolucent area apparently in the center, geometrically speaking, of the reactive portion suggests the differential diagnosis. This is the annular sequestrum of some authors. In Fig. 5 is seen the typical lesion in the neck of the femur, a slight variation from normal, but none the less recognizable by the small radiolucent portion in the osteoplastic reaction.

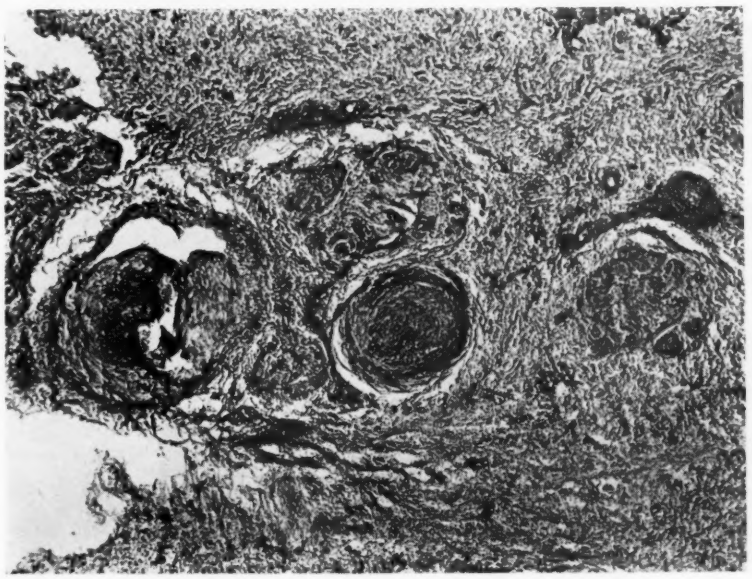

Fig. 7.—Specimen from right tibia of white boy, aged 3 years, who had had pain and swelling in the right leg for six months. Swelling was increasing and pain decreasing when the patient was seen. He had nocturnal pain, awakened, and cried out. Swelling and reddening with tenderness were present. The specimen is characterized by chronic fibrous tissue, obliteration of vessels, and scattered giant cells (×45).

Not illustrated because it seemed impossible to reproduce was a lesion showing in the lower portion of the radius of two months' duration. Here was seen the architecture of those shown, with this difference, that the density was much less and the cortical portion itself and the medulla had undergone little change. The small shadow of decreased density was located definitely without the cortex and entirely within the area of periosteal reaction. This was interpreted as an early lesion for the same reason that the patient shown in Fig. 3 is believed to have a late lesion because of the extensive organization. In cases of early lesions overexposure of the roentgenogram may be an aid in obtaining more significant material.

PATHOLOGY

The pathologic picture is one of chronic inflammation. This is in distinct contradiction to the work of Jaffe,[3, 4, 5] whose excellent presentations must be consulted by anyone interested in these lesions. Fourteen of the twenty-four patients seen were submitted to surgical correction.

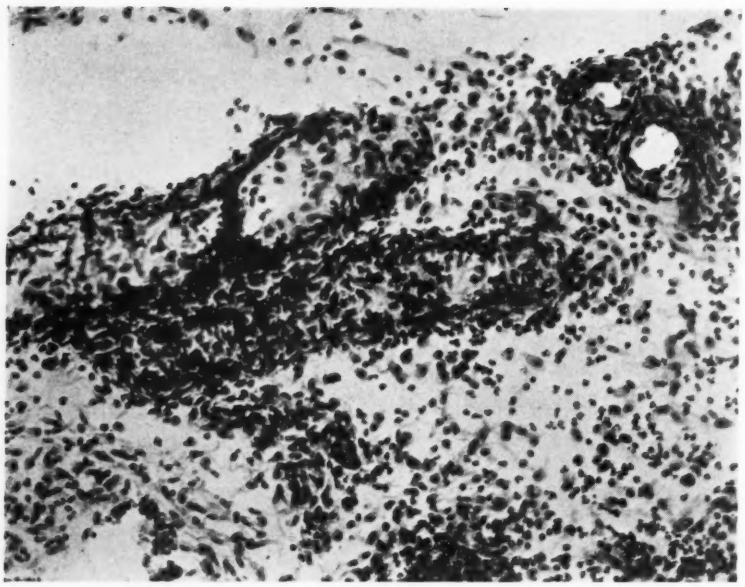

Fig. 8.—Specimen from left tibia of white girl, aged 5 years, who had complained of pain in the lower part of the left leg for three months. Ten months previously she had a "boil" on the upper outer portion of the left leg. She was said to have had a low degree of fever. A culture of *Staph. aureus* was obtained at operation. The lesion was seen surgically as 2 c.c. of purple granulation tissue, corresponding to the location in the roentgenogram. Microscopically, it was characterized by polymorphonuclear infiltration in fibrous tissue (×145).

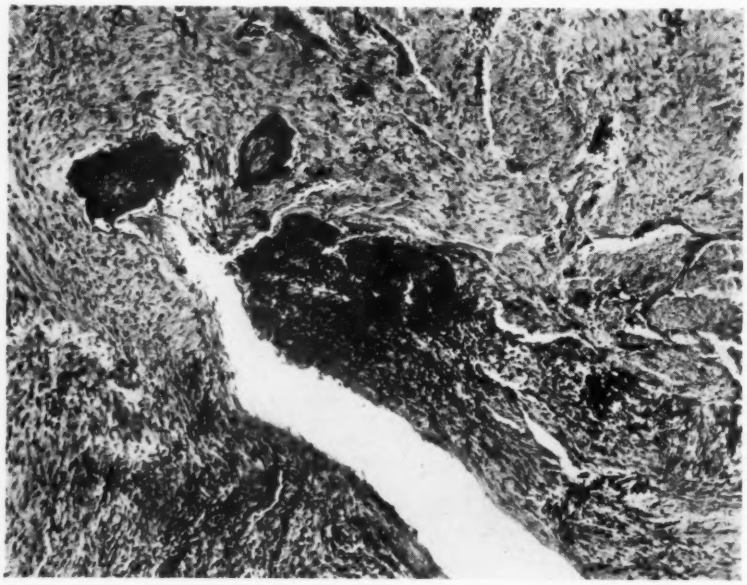

Fig. 9.—Specimen from right tibia of white man, aged 29 years, who complained of pain and swelling. Redness was occasionally present. Symptoms occurred with intermissions. Hot packs afforded some relief. Varicosities were present bilaterally. The specimen was characterized by dense regions of necrotic bone in chronic fibrous tissue and scattered round cell infiltration (×75).

In ten cases the lesions were seen microscopically by the pathologist as "chronic inflammatory tissue." Review of these sections revealed the picture as seen in Fig. 7, typically chronic fibrous inflammatory tissue with a few scattered giant cells and scattered collections of round cells. Obliteration of the vessels as shown here was well marked in all of these sections. Instances, as in Fig. 8, were also observed in which there was infiltration of polymorphonuclear leucocytes in fibrous connective tissue. Fig. 9 illustrates the destructive nature of the lesion, old necrotic bone seen in a field of chronic inflammatory fibrous tissue and scattered round cell infiltration. The roentgenographic findings in these cases were typical.

TREATMENT

The treatment of these patients was not uniform. Fourteen were submitted to operation. These obtained definite relief. One was given roentgen therapy and was much improved a year later. One was advised to undertake rest in bed and was improved both clinically and as seen by roentgenogram on repeated examinations. The final results are not yet determined in this case. Surgical excision is the procedure of choice, offering the best assurance of relief. Removal of the exciting portion is sufficient, only a small region being attacked. Further proof of the necessity of surgical intervention is found in those patients seeking relief, nine, ten, twenty-seven, and thirty-five years after onset. The operation is comparatively simple, exception to this statement being taken in two circumstances, first in those in which lesions are present in the neck of the femur and such places as the patella. There are perhaps others as difficult for this reason, but not yet encountered. Second, it is by no means with unpracticed marksmanship that one approaches accurately these lesions, minute as they may be and lying in the dense armor of bony tissue overlying them. Possibly, roentgen therapy may offer some benefit. The impression is, however, that the results will not be comparable to those of surgical excision.

COMMENT

Discussion of the causation has been avoided purposely to this point. Examination at necropsy of the external portion of these lesions failed to reveal any findings conforming to the usual picture of a new growth. The results of inflammation were evident in all of the tissue reviewed. In spite of the fact that in only one of these cases was there measurable fever, it is felt that inflammation is the basis of the lesion. Despite the fact that the patient seeks the dramatic curtain raiser for the onset of his complaints, nine of the patients in this group, or approximately a third, accurately noted that a fall or a bump, or, as in one instance, a puncture wound from a nail in the heel initiated the pain. In one case a bump to the forearm caused swelling, which had never subsided during the two months' interval between the bump and the

examination. It was in this instance also that the early lesion previously alluded to was seen in a roentgenogram. Eight of the patients of this report had had a previous focal infection such as chronic cervicitis, tonsillitis, a boil, typhoid fever or, as in one, a swollen painful knee (not the patellar lesion).

It is realized that both trauma and focal infection are not proved easily. However, two-thirds of all our cases may be accounted for as due to trauma or infection rather than to a neoplasm. Add to this that two of the patients had had their disease for twenty-seven and thirty-five years, and one feels that it more nearly follows the general picture of low grade inflammation than one of new growth as has been presented by Jaffe. The findings, as in Fig. 3, tend to support this view. *Staphylococcus aureus* was found in two cultures and micrococcus was found in two, all taken from the tissue at operation. Neither the age of the patient nor the duration of the disease apparently plays a part in the ability to find organisms. In the two cases in which staphylococcus was found the patients were at the ages of 5 and 22 years. The estimate of duration was ten and two and one-half months respectively. Micrococcus was found in patients aged 3 and 15 years, the duration of the symptoms being six months in the first case and five years in the second. Fig. 7 is from the former patient. Fig. 8 is from tissue of the patient aged five years with the duration of ten months.

No patient was included in this series who had a known concomitant bone lesion. That cortical abscess occurs in instances of chronic osteomyelitis is well known and has been commented on repeatedly by Phemister.[6, 7, 8] We agree with others in distinguishing this lesion from osteomyelitis of Garré, which is a symmetrical lesion in its roentgenogram. The eccentric position seen here is not present. Two roentgenologic projections should serve to distinguish the lesions.

Speculation as to the comparable frequency of Brodie's abscess seen in this review is possibly not fruitful; however, the similarity of the number of occurrences and of the pathologic pictures suggests that this may be the cortical counterpart of that lesion. Great powers for organization of defense are present in the cortical region, which is evidenced by the massive reaction as seen both roentgenographically and at operation. Further support may be gained from the fact that previous infection and previous trauma occur in approximately the same percentage of patients who have the disease.

One realizes that trauma is difficult to reconcile with lesions in such sites as the neck of the femur and those portions of the tibia opposed to the fibula. However, in no case of lesion of the femoral neck was a history of external force elicited. In those cases in which it was recorded, the lesion occurred in the tibia six times, in the radius once, in the os calcis once, and in the middle segment of the femur once, all regions accessible to direct force. Fifteen occurred on the right as op-

posed to nine on the left, and there was also a slightly greater number of male patients. One has the impression of a small lesion being overwhelmed by massive defensive mechanisms apparently present in the region of the cortex.

SUMMARY

Data on twenty-four additional cases of eccentric minute lesions of bone (cortical abscesses) are presented. The following observations support the hypothesis that the condition is due to trauma or infection rather than tumor.

1. Microscopic evidence of formation of tumor was not seen in fourteen of twenty-four cases in which specimens were examined microscopically.

2. Definite destructive and inflammatory changes, not only of a fibrous nature, but also of a more acute one, were observed.

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FASCIA LATA REGENERATION

Preliminary Report

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THE purpose of this communication is to show what happens to the fascia lata defect when a part or all of the fascia lata is removed in the performance of certain surgical operations.

I beg indulgence of the editors and the readers that I may be permitted to relate briefly the incidents which have led me to use fascia lata in many types of surgical procedures for sixteen years and the manner in which I came to discover what occurs in the defect from which the fascia lata is removed.

It was my good fortune and great pleasure to attend the clinic given by the late Dr. Scrimger of Montreal to a group of surgeons at the Royal Victoria Hospital during the meeting of the American College of Surgeons in 1926, at which time he demonstrated by operation the use of living fascia lata transplant sutures for the repair of inguinal hernia according to the technique of Gallie and Le Mesurier.[1, 2] The day of my return home I had to repair a large direct inguinal hernia in a woman. I used fascia lata for sutures, as I had seen it used by Scrimger, with special needles which I had brought from Montreal.

Since that time I have used fascia lata transplants in all recurrent inguinal hernias which I have repaired, all large inguinal hernias, direct and indirect, with wide internal oblique and transversalis aponeurosis defects, almost all incisional hernias, and all the large true ventral hernias. Earlier, I used fascia for the suturing of bones in some cases in which open operation seemed indicated to maintain the reduction of fractures, but soon gave that up. I have used it in operations for arthroplasty, ligament replacement, and tendon repair. It was in one of the latter cases that I was fortunate enough to discover what happens in the way of spontaneous replacement of the fascia lata when I had both the privilege and chagrin of being compelled to reoperate upon a patient for repair of a ruptured supraspinatus tendon, the first operation being a failure. Since that time I have had the pleasure of dissecting out and seeing for myself, as well as for my associates, that which occurs in four more instances.

Except in Case 1, I had photographs made of the regenerated fascia during and after removal at operation. W. P. L. McBride, the pathologist of our hospital, was not equipped to do some of the technical micro-

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scopic studies which I desired, but was very kind in helping me locate someone who could do this for me. Some of the technical requirements, as will be later shown, were of considerable magnitude. Ernest W. Goodpasture, professor of pathology of Vanderbilt University, very kindly consented to aid me and made the microscopical sections, photomicrographs, and pathologic studies in this report, for which I am very grateful.

CASE 1.—A white man, J. J., a carpenter, aged 65 years, short, robust, obese, came to me Jan. 10, 1938, for repair of a ruptured supraspinatus tendon which he had received from an injury to the left shoulder when a scaffold fell with him on Dec. 7, 1937, causing the point of the shoulder to strike a board on the ground. Operation was performed May 16, 1938. The supraspinatus tendon was exposed by a straight Codman incision downward from the acromial process of the scapula. The avulsion was so great that I decided to attempt reconstruction by fascia lata sutures. An incision six inches long was made through the skin and subcutaneous fat on the lateral surface of the left thigh, and the fat brushed aside with the knife, exposing a clean surface of strong fascia lata two and one-half inches wide, the full length of the incision. Two strips of fascia each one-half inch wide and six inches long were removed. These fascia lata sutures were passed through drill holes beneath the superior facet of the humerus and anchored to the avulsed end of the supraspinatus tendon with black silk. The wound was closed in layers with 00 plain catgut for the deeper layers and fine dermal for the skin. The arm was maintained in abduction.

On the sixth day infection was apparent in the deeper parts of the wound, but not in the skin. On opening the lower angle of the wound a large amount of thick, purulent material was evacuated, and in it were some silk sutures. All of that stock of silk in the operating room was cultured and found to be contaminated with a hemolytic staphylococcus. The wound was Dakinized and the infection subsided in a few days after all the silk sutures came away. I then realized that the operation was a failure. The arm was carried in an aeroplane splint and frequent physiotherapy was given the extremity to prevent further atrophy until Jan. 10, 1939, when a second operation was done for the repair of the tendon.

I was compelled again to use fascia lata because of a greater defect than before in the musculotendinous cuff, and decided to open the same incision on the thigh for the fascia. I found that the two margins of the fascia lata had spread apart three inches in the center. Much to my surprise and amazement, connecting these two margins of full thickness fascia lata was a smooth layer of fascia which completely covered and obscured the muscles and appeared to be one-half as thick as the original fascia lata, or one-half as thick as the fascia margins. An incision was made along the lateral edge, in order to take some full thickness fascia lata for this operation, and in freeing the regenerated or new fascia lata from the old, I observed that this new fascia was a real layer with the thickness of a thin kid glove and was not more adherent to the muscles than was the normal fascia lata. I realized that it could have been used for sutures as well as normal fascia lata, had it been double or had the strips been taken twice as wide and folded one side on the other. I was so intent on the operation before me that I neglected to photograph this new fascia, or to take sections for biopsy. The following day I realized that I had found something I had not known before, and my curiosity was aroused to see if this regeneration might occur on other patients from whom I had removed fascia lata for various operative and plastic procedures. It was my pleasure within a few months to have the opportunity of exploring the second case.

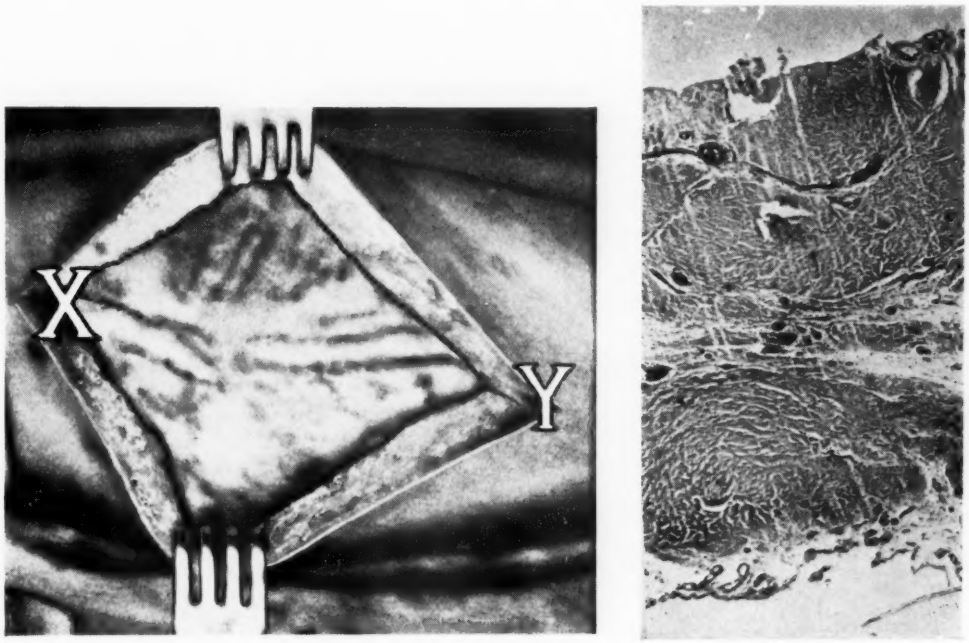
The histologic study of fascia lata is so interesting and pertinent to these cases I feel that I should make a few brief remarks here about normal fascia lata before proceeding further with the next case report. Fig. 1 shows normal fascia lata to have three distinct layers; a middle longitudinal layer which is the stronger one, and two transverse layers, the outer and inner layers which are the weaker ones. Both together equal or surpass the middle one. Further explanation is found under the heading Comments.

Fig. 1.—Normal fascia lata cut transversely to the strong middle longitudinal layer, and therefore parallel to the inner and outer transverse layers. (×100.)

Case 2.—A white man, L. H., aged 42 years, tall and slender, reported to me on Aug. 13, 1939, with a right direct recurrent inguinal hernia which I had repaired with fascia lata sutures taken from his right thigh on Nov. 11, 1937, according to the technique of Gallie and Le Mesurier,[1, 2] using two strips of fascia lata each five-eighth inch wide and six inches long. The patient had a cleft palate and a chronic upper respiratory infection. In spite of the usual precautions following the first operation he developed an acute respiratory infection and a distressing cough the fourth day, which continued for ten days. This was probably the basis for the recurrence of the hernia. Operation was again performed on Aug. 15, 1939. On reopening the right thigh through the old incision for removal of more fascia, I found that the two margins had not retracted as in Case 1, but the two margins were reunited from one end of the incision to the other. The line of union of the two margins was so firm that it gave the appearance that the fascia margins had

been joined by suture, and extensive fibrous tissue proliferation similar to a keloid formed the union (Fig. 2*A*). I removed a specimen from this scar. Sections were cut before I could explain to our pathologist my desire to have it sectioned transversely. I believe it was cut obliquely and it shows two thick layers with much proliferation of fibrous tissue and numerous blood vessels. The middle longitudinal layer is probably absent in this area of regeneration (Fig. 2*B*).

Now, having observed these two patients, I was determined to look further at the fascia lata of patients from whom I had removed living sutures and fascia grafts.



A. *B.*

Fig. 2.—*A*, Dense line of union from *X* to *Y* of fascia lata as though it had been approximated by suture. *B*, Two dense layers of regenerated fascia lata form the union. (×45.)

CASE 3.—A white man, C. R., aged 48 years, medium build, slender extremities, was referred to me on Jan. 26, 1939, for the repair of a ventral hernia. I performed the operation for the cure of the hernia on Jan. 28, 1939, using three living fascia sutures one-half inch by seven inches which were taken from his right thigh. The patient was called to my office on June 25, 1939, and I persuaded him to let me reopen his thigh to see what had happened to the fascia lata defect. He kindly consented, and four days later I explored the defect by excising the old scar in the right thigh for a distance of six inches. When the skin and subcutaneous fat were freed from the fascia lata there was found a complete union of the margins of the fascia lata as though the two edges had been sutured together (Fig. 3*A*). And this ridge of union the length of the incision was twice as thick for a breadth of three-quarter inch as was the fascia lata anywhere else, quite identical to Case 2. A block of fascia two inches long was secured from the middle region of this scar, taking some of the normal fascia on each side (Fig. 3*B*). The wound was closed

in layers and a tight pressure bandage applied. Sections and photomicrographs made by Goodpasture show (Fig. 3*C*) at the extreme left a small area of normal fascia lata with its three layers. Extending across from that is a dense body of fibrous tissue which appears to be the extension and proliferation of the inner and outer transverse layers which fuse into one. The normal fascia on the other side does not show on the right since none was taken with the specimen at this level.

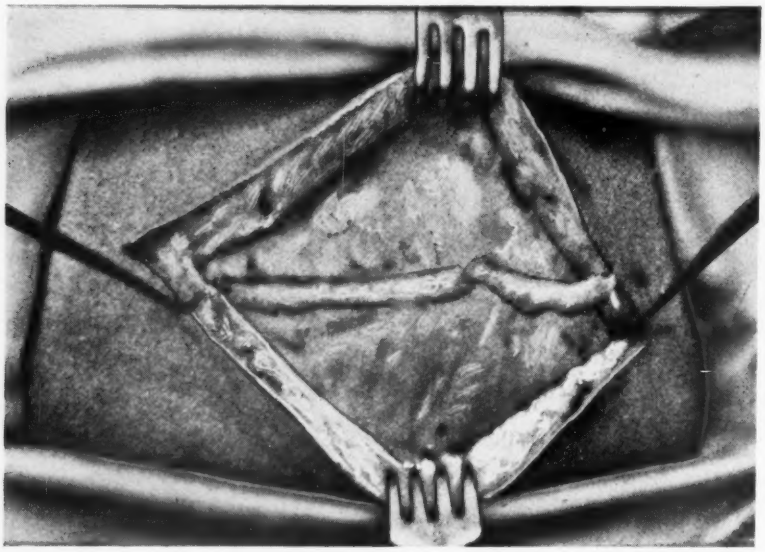


Fig. 3*A*.—Dense layer of fascia lata like a rope between the two skin hooks is the line of union.

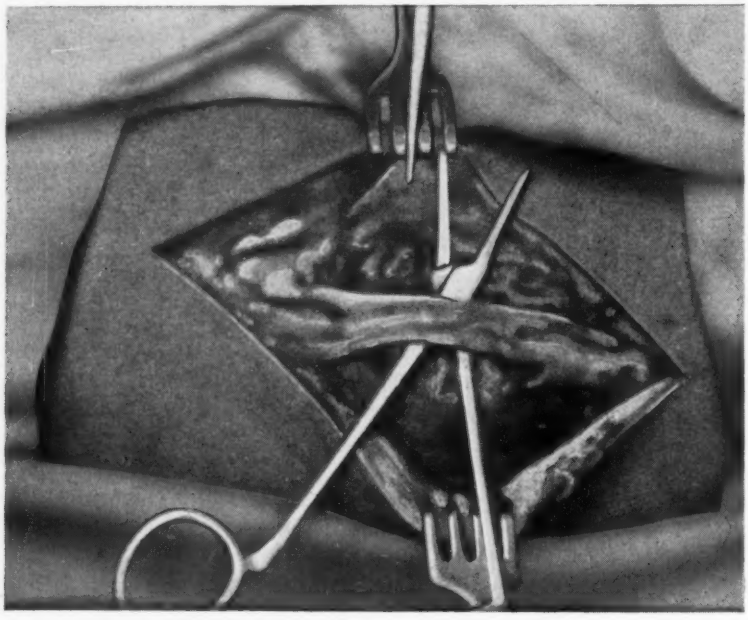


Fig. 3*B*.—Regenerated fascia lata union removed for biopsy.

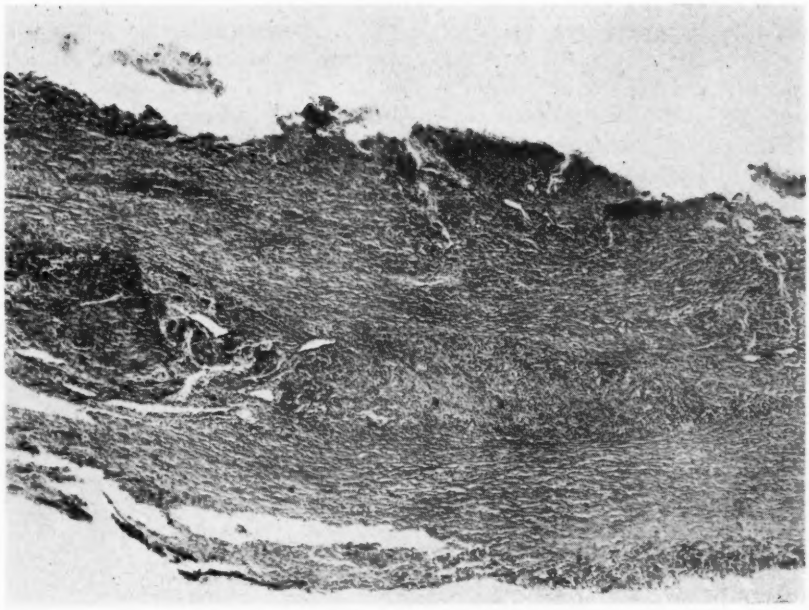


Fig. 3*C*.—Cross-section line of union. There is a margin of normal fascia lata on the left with its three layers. All tissue to the right is made up of the inner and outer layers and represents regenerated fascia lata, the middle longitudinal layer being absent. (×45.)

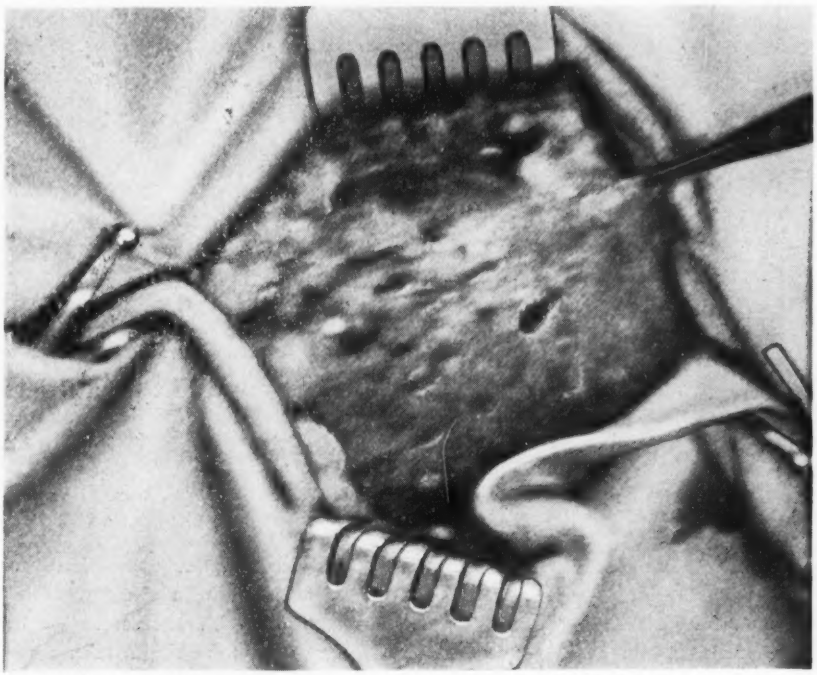


Fig. 4*A*.—Surface view of regenerated fascia lata.

CASE 4.—A white woman, L. H., a housewife, aged 65 years, robust, obese, upon whom I had performed the operation for the cure of ventral hernia Aug. 18, 1940, using three strips of fascia lata five-eighth inch by eight inches for sutures, reported to me at my request on May 2, 1941, at which time I explained to her why I desired to explore her thigh at the site from which I had removed the fascia lata. She readily consented, and on May 5, 1941, under local anesthesia, the old scar on the right thigh was removed by excision; the skin and subcutaneous tissue were dissected back to free widely the fascia below (Fig. 4*A*). The medial border of the fascia lata had retracted to about the midline of the thigh. The lateral border had retracted externally, enough to make an opening four inches wide in the middle.

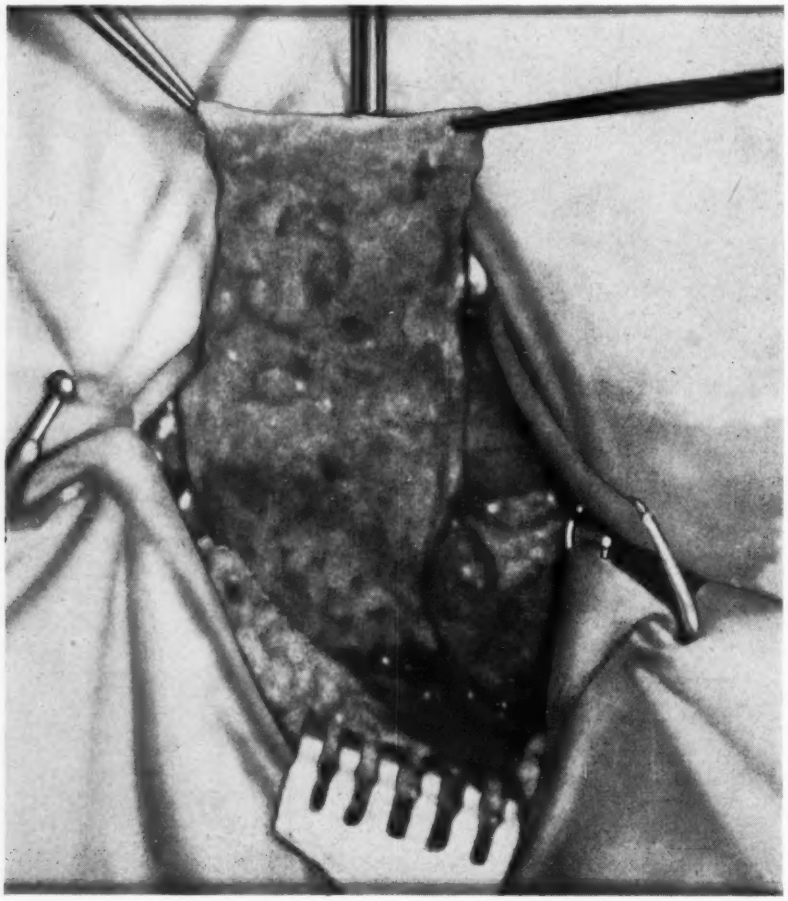


Fig. 4*B*.—Transverse flap of fascia lata dissected up with 1 cm. normal fascia lata at the top between the two hemostats.

This elliptical defect throughout its entire length was completely filled in by a new layer of fascia lata, grayish-white, glistening, and smooth in appearance, and it was one-half the thickness of the normal fascia lata. A block three inches by five inches of this fascia lata was removed transversely across the thigh, taking one-half inch of the normal fascia lata from the medial edge (Figs. 4*B*, 4*C*, and 4*D*). It was impossible to cut with this block any normal fascia lata on the lateral edge because it had been removed externally close to the border of the rectus femoris muscle

in obtaining the sutures. This regenerated fascia lata had the identical gross appearance of that in Case 1, not more attached to the subcutaneous fat than was the normal fascia lata, and loosely attached to the muscles by occasional fine trabeculations as is found in normal fascia lata.

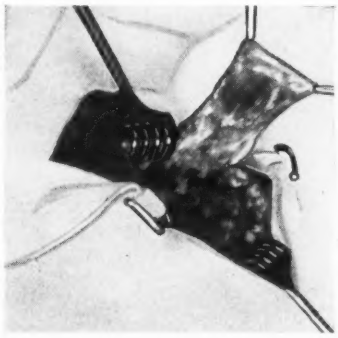


Fig. 4*C*.—Smooth vastus muscle shows beneath, undisturbed.

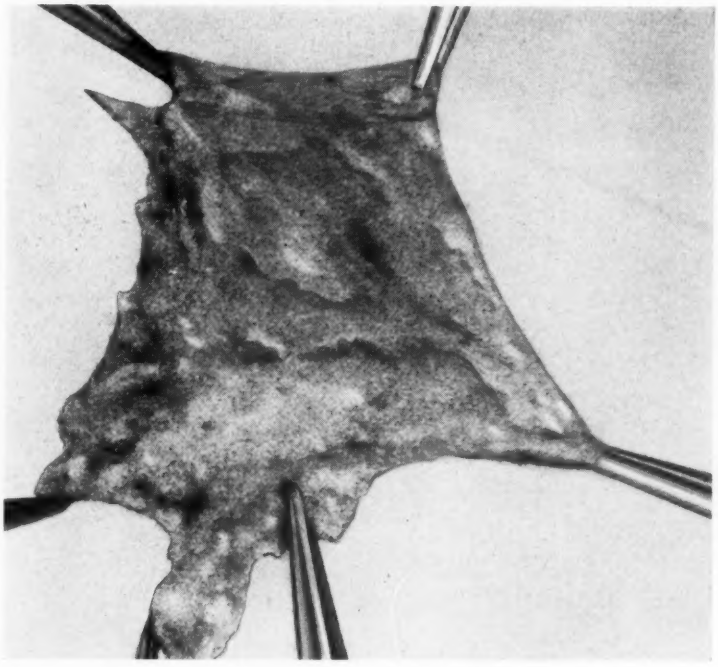


Fig. 4*D*.—Normal fascia lata between the two hemostats at the top. The remainder is regenerated fascia lata.

At this stage of the investigation it was apparent that I had observed two different ways in which fascia lata regenerated. In the two slender patients there was apparently no separation of the fascia edges, for they reunited together snugly; whereas in the two obese, robust, and muscular patients there was a wide separation of the fascia lata edges, but the

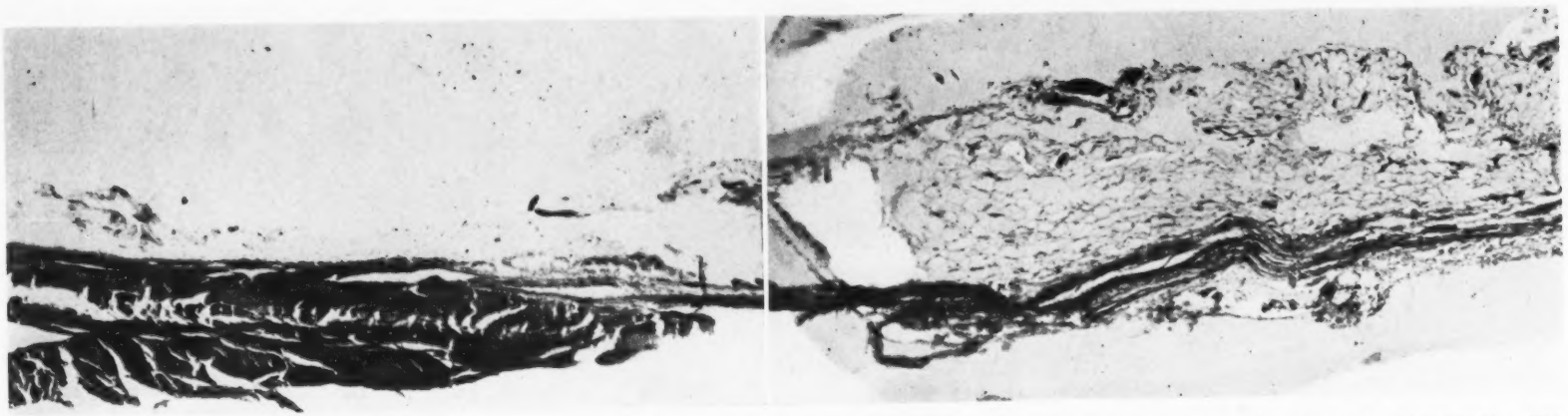


Fig. 4*E*.—Normal fascia lata in the left half. Regenerated fascia lata in the right half. The external layer extends across in continuity. The inner layer has been torn loose from the left half and is curled back just to the right of the middle. Note the dense fascia bundles of the middle layer in the left half. (×22.)

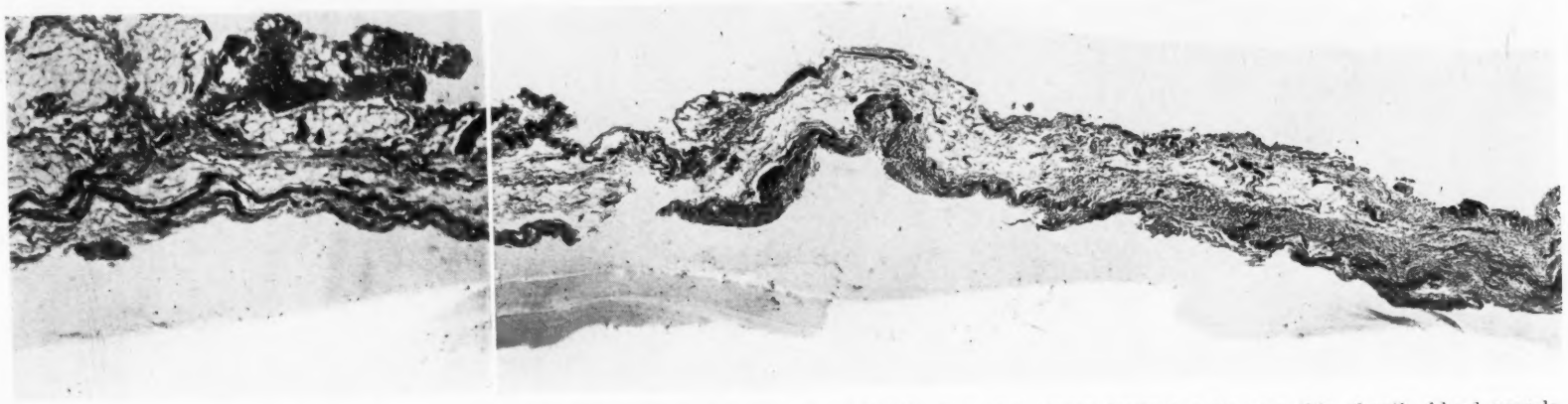


Fig. 4*F*.—Inner and outer layers of regenerated fascia lata extending across in continuity from 4*E*. Each layer has its own thin sheath, blood vessels, nerve supply, and intervening layer of adipose tissue. The middle longitudinal layer is absent. (×22.)

Fig. 4G.—Continuation of the two layers as in 4F. (×22.)

Fig. 4H.—Transverse section at a different level from 4E, with greater magnification (×38), shows in the left two-thirds the distinct layers of normal fascia lata with the longitudinal layer in the middle, its bundles being cut transversely. Only the inner and outer transverse layers, whose bundles are cut parallel to their fibers, extend across to form the regenerated fascia lata.

intervening defect was covered by fascia lata which was thinner than normal fascia lata. Except for this, it had all the gross characteristics of normal fascia lata.

I then decided that I should have cross-section microscopic studies made in tandem of this entire specimen cut on edge. I found it very difficult to find a pathologist who would or could do this, but when I went to Dr. Goodpasture with the gross specimen and my problem, he quickly found a way to do it. The specimens and photomicrographs are a work of art (Figs. 4*E*, 4*F*, and 4*G*). They show that in all probability it is the outer and inner layers of fascia lata which regenerate and extend by continuity across the previous defect. Fig. 4*H*, made at a different level from 4*E*, shows clearly the three layers of normal fascia lata in the left two-thirds, whereas, in the right third it shows only the inner and outer layers which extend across to form the beginning of the regenerated fascia lata.

If we assume that the inner layer has by accident been torn away from the inner half of 4*E* and is shown curled back in the right half of 4*E* near the middle, then we feel certain that 4*E* would also show the three distinct layers throughout its breadth with the middle longitudinal layer extending nearly halfway across and being very dense. The external layer extends directly across from 4*E* and runs in continuity to the end of the specimen in 4*G*; the inner layer which starts from the curled-up portion in Fig. 4*E* extends straight across in continuity throughout the length of the specimen through 4*G*. There is some adipose tissue on the outside of the upper layer and each layer has its own blood vessels and much intervening collagenous fibrous tissue.

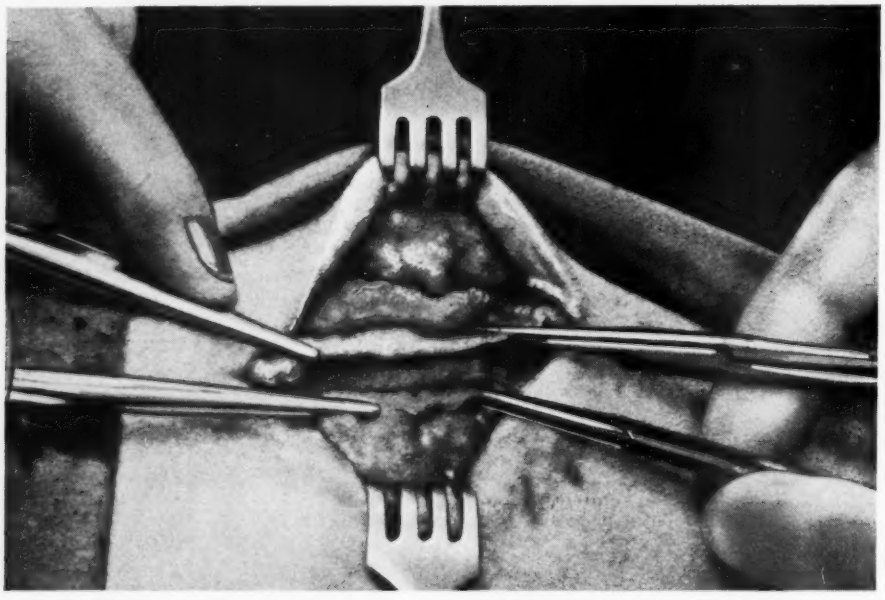


Fig. 5*A*.—Distinct layer of regenerated fascia lata incised.

Case 5.—A white male, E. T., aged 35 years, a college professor, medium build, slightly adipose, from whom 12 years before I had removed all the fascia of the right thigh for the purpose of a knee arthroplasty on his brother of the same blood group. At the time I thought the brother had no more fascia lata of his own available, because of the two previous arthroplasties which I had performed,

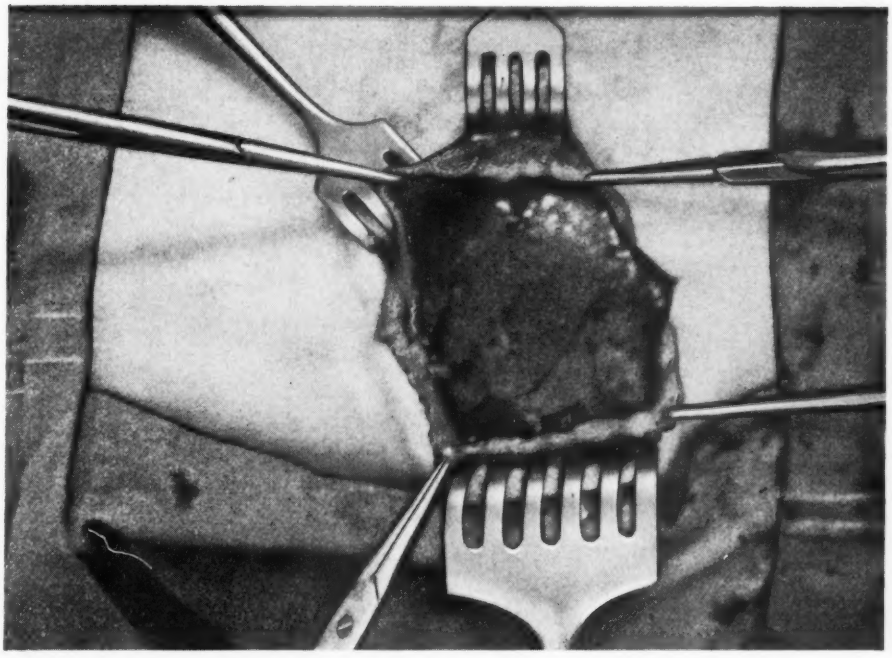


Fig. 5*B*.—Regenerated fascia lata flaps dissected up showing smooth vastus muscle below.

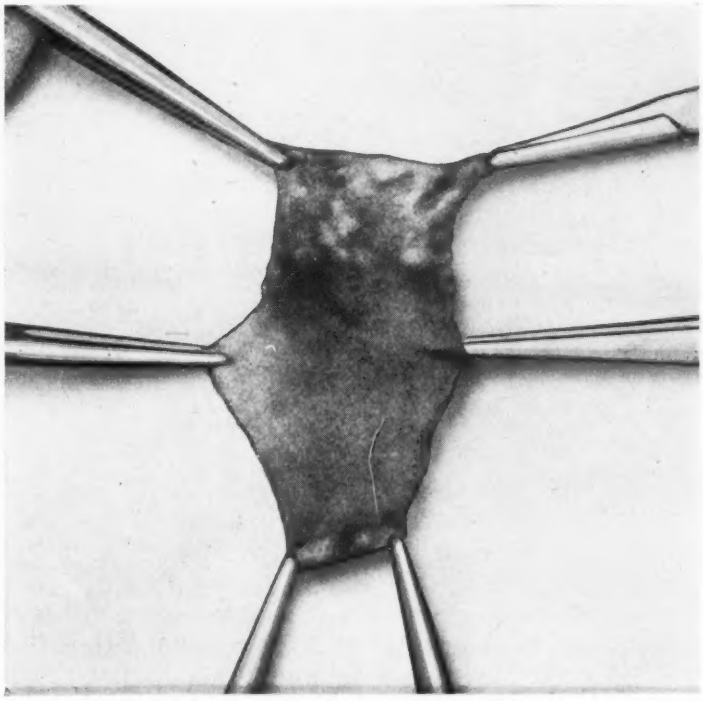


Fig. 5*C*.—Regenerated fascia lata specimen.

for in so doing I had removed the fascia lata from both of his thighs. I explained my purpose in desiring to explore the thigh of the professor to determine what had occurred. He consented, and on Sept. 27, 1941, under local anesthesia, I made a three inch incision in the middle of the old twelve inch incision, and after freeing the subcutaneous fat I found a distinct, smooth, and firm fascia lata. By dissecting

Fig. 5*D*.—No herniation of the muscles, although all fascia lata was removed twelve years before.

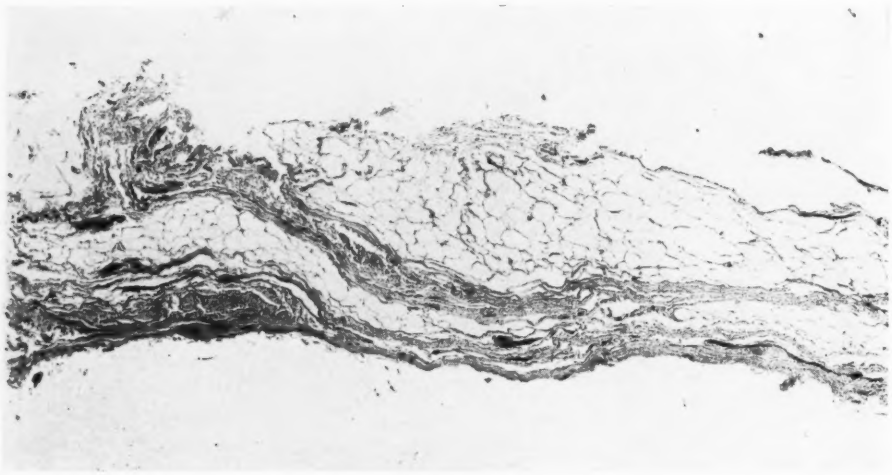


Fig. 5*E*.—Cross section at right angles to the long axis of the thigh shows two distinct layers of fascia with collagenous fibrous tissue and adipose tissue. (E. W. Goodpasture) (×22.)

widely to either side the skin and subcutaneous fat off the fascia lata, I could visualize clearly an area of the fascia four inches by five inches. This fascia was incised longitudinally and the margins freed from the muscles in both directions (Figs. 5*A* and 5*B*). It was loosely attached to the thigh muscles as is fascia lata normally by fine trabeculations. It was three-fourths as thick as a well-developed layer of normal fascia lata and a sheet of this fascia doubled would have been excellent for arthroplasty, and could have been used singly in an emergency. (Fig. 5*C*). I have removed fascia lata for sutures in apparently normal patients in

whom the fascia lata was no thicker than the regenerated fascia lata in this case. There was no herniation of the muscles (Fig. 5*D*). Sections and photomicrographs of this specimen (Fig. 5*E*) show two distinct layers with their respective blood vessels and adipose tissue. Goodpasture notes that the stain with aniline blue shows the regenerated fascia is composed of collagenous fibrous tissue similar to, though not as dense as, that in normal fascia lata. He also makes the point that the specimen appears much more substantial grossly than microscopically.

COMMENT

Nothing can be found in the literature concerning what happens in the defect created by the removal of fascia lata. Gallie[3] makes the statement that one often wonders what the late effect may be of removing strips of fascia lata from the thigh, and admits that although he always sewed up the rent made by the removal of the living sutures, he could find no functional difference in his patients and those of his colleagues in whom the edges were not sutured together. He states that if the fascia is left open one can feel the edges widely separated, and there is a definite bulge of the vastus muscle through the opening, but there is no discomfort or noticeable loss of strength, and it does not seem to matter whether the fascia is closed or not. He makes no suggestions, however, as to the possibility of the regeneration of the fascia lata to fill the defect.

I have removed fascia lata from about 300 individuals. I have occasionally noticed a bulge of the vastus muscle for a few months, but after six months it has disappeared in every patient that I have been able to follow up.

As for the reason for this regeneration, none can be given except that of mechanical demand. Gratz[4] points out that while fibrous tissue is found in greater or lesser degree in all organs, it predominates in certain locations, and where support is the chief function, fascia develops. It would seem then that when fascia lata is removed and herniation of the muscle occurs, there is demand for more support, and the fascia lata regenerates in reply to this demand. The extent of the regeneration of fascia lata can best be determined by comparing photomicrographs of the regenerated fascia of Case 5 with normal fascia lata (Fig. 1), of J. M.

Kleinschmidt's histologic studies[5] on the free transplant of fascia lata of rabbits gives more light on what may happen in the way of fascia lata regeneration in man than anything I have read. He showed that normal fascia lata contains three distinct layers, each within its own sheath and its own blood vessels, and the three within a common denser sheath. The middle layer is the strongest and runs longitudinally. The inner and outer layers are weaker and their fibers run transversely at an angle of 90 degrees to those of the middle layer. This arrangement accounts for the fact that the greater tensile strength of fascia lata is lengthwise. Kleinschmidt also showed that if fascia lata was transplanted into a quadriceps defect with the thicker longitudinal fibers placed transversely to the long axis of the thigh muscles and the two

layers of transverse fibers were made to assume the longitudinal pull, then the two transverse layers at the end of three months grew in thickness and strength to the extent that they were like a tendon or aponeurosis, whereas the previously strong longitudinal fibers atrophied. He also showed that if a transplant of fascia lata was sutured into a quadriceps defect with the longitudinal fibers remaining lengthwise, those fibers at the end of three months became stronger resembling a tendon, whereas the transverse fibers almost disappeared. And by other experiments with rabbits he showed that if fascia lata was taken up and replaced in its normal position with the one layer of longitudinal fibers running longitudinally and the inner and outer layers transversely there would be no change at the end of three months in any of the layers.

In another treatise by Kleinschmidt[6] on the clinical application of free autoplastic fascia lata transplants in man, he utilizes to great advantage the information gained from his animal experiments in placing the fascia lata transplant so the stronger longitudinal fibers would be in proper position to take up the greater tension required of the transplant. He further stated that removal of fascia lata in the human being never left any functional defects, and besides, when any great amount was removed, as is often necessary in certain operative procedures, resuturing of its margins would be impossible. In some cases he noticed a temporary muscle bulge in the thigh which disappeared in a short while.

It will now be seen that the conclusions from Gratz's work on animals are similar to the conclusions reached by Kleinschmidt, also working on animals. And they explain in a measure the findings of the fascia lata regeneration of the cases in this report.

In Cases 2 and 3 the fascia lata margins at the time of operation were separated too much for approximation by suture, yet they approximated themselves by dense fibrous tissue formation in a fashion in order to form such a close line of union. It is my belief that the strong, longitudinal pull required of each fascia margin had a tendency in these slender muscular individuals to pull together as would the strings of a violin when made taut. We can liken it to the self-approximation which often occurs in the midline of the prethyroid muscles following partial thyroidectomy whether they are sutured together or not.

The explanation for the regeneration of fascia lata in the obese patient in which the fascia margins are further separated by the bulging vastus muscle is another story. And so it is with the fascia lata regeneration in the individual from whom all the fascia lata has been removed. This constitutes the most interesting part of the study. I believe it is the inner and outer transverse layers that regenerate. This seems reasonable in the light of the knowledge gained from Kleinschmidt's work, and from the study of the microscopic sections presented in this report. It would appear that the chief function of these two layers would be to reunite the separated fascia margins in Cases 1 and

4, but in Case 5 no explanation at this time seems feasible that would omit any layer. I hope in a future report to clear up some of these questions.

CONCLUSIONS

1. Fascia lata regenerates to fill the defect from where fascia is removed.

2. In the thin or slender well-muscled individual the fascia lata margins approximate to close the rent by rapid and thick formation of fibrous tissue which is in all probability derived from the inner and outer layers.

3. In the adipose patient the fascia margins retract further and perhaps for a short time allow a theorectical muscle herniation through the rent, but very soon the defect is filled by a new fascia lata one-half the thickness of the old fascia lata. This is thought to be the regeneration of the outer and inner layers of the true fascia lata. Further study will be made in a subsequent report.

4. When every iota of fascia lata is removed, new fascia lata of from one-half to two-thirds the thickness and tensile strength of the previous fascia lata regenerates to cover the whole area normally covered by fascia lata, and it may well be used again for fascia sutures and transplants.

5. This regenerated fascia lata serves all the purposes of true fascia lata in making a sleeve for the muscles and preventing herniation.

6. To know that fascia lata regenerates as shown here should encourage military surgeons to use fascia lata freely when needed in the great amount of reconstructive surgery that necessarily will be required for the injured men of our armed forces.

To Dr. E. W. Goodpasture I am indebted more than words allow me to express for his very valuable work in preparing these specimens. I am also deeply grateful to Dr. J. B. Wilkes of my staff who aided me in compiling information and bibliography.

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SULFATHIAZOLE TOXIC NEPHROSIS AND KIDNEY DECAPSULATION

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SINCE the extensive use of the sulfonamide drugs there have been many cases of renal complications, some of them resulting fatally. Reports of these fatal cases and also experiments carried out on rats and other animals seem to indicate that two types of renal changes occur.

In one type the renal changes are due to the drugs, causing concretions or precipitates. These crystals or concretions then produce a blocking of the renal tubules, the kidney pelvis, or the ureter. It is a common observation that a patient receiving a large dose of sulfathiazole or sulfadiazine may show no demonstrable renal complications, even when the urine shows a large deposit of crystals. It has been our experience that when blockage by crystals does occur, it usually occurs in the kidney pelvis which is of a "dysuric" type,[1] when the ureteral orifices are smaller than usual, or when some congenital or acquired malformation is present.

Various workers have failed to find crystals in kidneys removed at autopsy following death presumably due to the sulfonamides. Therefore, there must occur another renal change which produces the oliguria, anuria, and uremia complex which appears.

Prien and Frondel[2] report five autopsy cases following sulfathiazole therapy. In these, there was renal failure which could not be ascribed to the disease under treatment. Sections of the freshly removed kidneys were prepared by frozen section technique (a technique whereby there was no chance for solution and disappearance of crystals to take place). In three of these five cases, they failed to find crystals. Death in these three cases was not due to tubular obstruction by crystals, even though the patients died of uremia. The histologic changes which were present in these nephroses of kidneys not obstructed by crystals were degeneration, necrosis, and edema. These same changes also have been reported in other organs of the body following death from sulfathiazole.

Loewenburg, Sloane, and Chodoff[3] report a personal communication from H. F. Flippin to the effect that no uroliths were found in sixteen autopsies of patients receiving sulfathiazole. Long, Haviland, Edwards, and Bliss,[4] in their article on toxic manifestations of the sulfonamides, believe that anuria is due to a true toxic injury of the tubules, probably similar to that in mercury bichloride poisoning.

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These reports indicate that renal failure from sulfonamides is not due necessarily to obstruction of the renal or ureteral channels by crystals but may be due to another factor which may be toxic in nature.

The measures used in the treatment of renal complications are the withdrawal of the drug, alkalinization, forcing of fluids, by mouth or parenterally, and local heat or diathermy to the kidneys. One should guard against allergy or hypersensitivity when using the drug. When these simple methods fail, the treatment has to be more drastic. It is then that ureteral catheterization is done for the purpose of washing out the concretions if present. However, when the renal complication is of the toxic type, the ureteral catheterization and washing of the kidney pelvis often does little if any good. It is in a case of this type that surgery offers the patient a chance of recovery, as it does in other cases of nephrosis which are reported.

Since the advocacy of decapsulation by Harrison, in 1896, and by Edebohls,[5] in 1898, a large number of cases in which decapsulation was performed has been reported. Many of these have been done for acute nephrosis with anuria. The causes of the nephrosis are many. The decapsulations have been unilateral and bilateral. At times a nephrotomy also has been done.

The following is a case history of a patient suffering from anuria, complicating the administration of sulfathiazole. The condition became desperate due to what appears to have been a "sulfa-nephrosis."

G. S., aged 44 years, was admitted to St. Louis City Hospital, March 1, 1943, with a chief complaint of inability to urinate. Two and one-half days previous to admission he was given sulfathiazole, 15 gr., every four hours, for an upper respiratory infection. Sixteen hours later he began to pass grossly bloody urine. He was passing only small quantities, and during the eighteen hours previous to admission he was unable to pass any urine.

The physical findings were negative essentially, except for a slight elevation of temperature, 101° F., and moderate tenderness over both kidneys. There was no muscle guard. The blood pressure was 142/90. A urethral catheter was introduced and only about 15 c.c. of grossly bloody urine obtained. It contained no crystals or organisms. The nonprotein nitrogen was 36 mg. per cent. The blood sulfathiazole concentration was 2.6 mg. per cent. X-ray diagnosis of the chest was negative. On the plain abdominal film the kidneys appeared moderately enlarged. Fluids were forced by mouth and parenterally. Alkalies were given and the patient began to vomit. March 3, 1943, his nonprotein nitrogen was 48 mg. per cent. Cystoscopy was done and ureteral catheters could not be passed. Ureteral meatotomies were done. Forcing of fluids was continued by mouth and parenterally. On March 4, 1943, carbon dioxide was 44 mg. per cent and nonprotein nitrogen 68 mg. per cent. The patient was vomiting everything and showing generalized edema. He was given a low spinal anesthetic, and attempts to catheterize the ureters again failed. They appeared to be edematous as were all other structures.

At 8:00 P.M. on March 4, 1943, a left renal decapsulation and nephrostomy were done since the illness was progressing rapidly. The tissues were markedly edematous

and swollen in appearance. As the capsule was removed, the kidney was seen to expand in size. The kidney pelvis contained some blood. A nephrostomy tube was inserted. Within a few hours urine began to pass through the nephrostomy tube, and the dressings were saturated with urine. About twelve hours after operation the patient had passed about 500 c.c. through the nephrostomy tube and 200 c.c. through the urethral catheter. The subsequent urinary output was as follows: first 24-hour period, 1900 c.c. through the nephrostomy tube, 1750 c.c. through the urethral catheter; second 24-hour period, 1500 c.c. through the nephrostomy tube, 1800 c.c. through urethral catheter; third 24-hour period, 700 c.c. through the nephrostomy tube, 825 c.c. through the urethral catheter; fourth 24-hour period, 1475 c.c. through the nephrostomy tube, 1360 c.c. through the urethral catheter. The blood nonprotein nitrogen was 38 mg. per cent on March 6, 1943, 21 mg. per cent on March 8, and 22 mg. per cent on March 13.

The generalized edema subsided rapidly and had disappeared completely on the third postoperative day. The urethral catheter was removed on the fifth postoperative day and the nephrostomy tube removed on the sixth postoperative day.

An intravenous pyelogram on March 25 revealed a normal right kidney pelvis and ureter and a slight dilatation of the left kidney pelvis and calices. Each kidney appeared to have equal and good function. Intravenous pyelography was not done before surgery because of the danger of administering diodrast in an anuric patient, and because we felt it would not be excreted and thereby not add to our findings.

The patient was dismissed from the hospital on March 29, 1943, by which time the wound had healed satisfactorily.

Even though we feel convinced that the operation saved the patient's life in the preceding case, we do not mean to suggest that every patient with sulfa-nephrosis should be operated upon.

We do suggest, however, that a patient suffering from acute sulfa-nephrosis should not be allowed to die from anuria and uremia without renal decapsulation and nephrotomy having been tried. At least it should be tried if the patient is not relieved by ureteral catheters and forced fluids, or if ureteral catheters cannot be passed. If the decapsulation and nephrotomy are done early, before kidney damage is too marked and other tissue changes have taken place, a much better chance of recovery can be expected. Following this type of nephrosis there is a great intracapsular pressure which does decrease kidney function to a marked extent. The decapsulation relieves the pressure and edema, and then allows restoration of the cells and function to reoccur.

SUMMARY

1. A case of anuria in uremia caused by the action of sulfathiazole and relieved by unilateral decapsulation and nephrotomy is presented.

2. Anuria during sulfathiazole therapy can be due to a toxic nephrosis or due to tubular obstruction by crystals.

3. Decapsulation is indicated in those cases of sulfa-nephrosis not relieved by conservative measures.

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ABDOMINAL PUNCTURE AS A DIAGNOSTIC AID

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THE value of abdominal puncture or paracentesis in the diagnosis and prognosis of intra-abdominal inflammatory conditions has been well described recently. Various investigators have reported it to be a reliable means of identifying the several types of peritonitis in children by the presence of bacteria in smears. Steinberg,[1] with an excellent review of these reports, advocated study of the peritoneal fluid obtained by aspiration as to cells, bacteria, and other substances. With the information obtained from a single smear he has been able to differentiate the irritative from the infectious processes of the peritoneum, and to establish the prognosis with some accuracy. Hill, O'Loughlin, and Stoner[2] demonstrated that in experimental obstruction in dogs, strangulation could be diagnosed within four hours after onset by the aspiration of characteristic reddish brown fluid from the peritoneal cavity. Our experience fully supports the importance of this procedure in the presence of peritoneal inflammation.

Neuhof and Cohen,[3] in 1926, reported the use of abdominal puncture not only for inflammatory conditions but also for the diagnosis of internal injury following trauma. Since that time a number of articles have been written on visceral damage following nonpenetrating injury to the abdomen but we have found only one reference to diagnostic puncture. Wright and Prigot[4] employed it in fifteen cases of ruptured spleen with positive findings in thirteen. They believe it is inexcusable to omit this diagnostic procedure where intra-abdominal complications are suspected. Since this is the type of patient in which it is of greatest value, abdominal tap deserves a great deal more attention in emergency cases where prompt and correct decision so often is the margin between life and death.

The technique is very simple. The site for puncture is chosen according to clinical impression. For example, if a ruptured spleen is suspected a tap is made in the upper left quadrant. Novocain infiltration is carried down to the peritoneum, and through this area an 18 gauge needle is slowly introduced into the peritoneal cavity. Fluid, if present, is aspirated by syringe. Negative findings in one area do not preclude positive results at another point.

At first thought it is natural to fear pushing the needle into the bowel. One has only to remember that force and counter pressure are

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necessary to insert a much finer needle through the bowel wall during intestinal suture to understand that this danger is almost nonexistant. We have seen no untoward effects following abdominal puncture in several hundred cases. In several patients operated upon immediately after tap, careful search has been made for bowel injury. None has been found. In many patients tapped but not operated upon there has been no suggestion of even a local peritonitis which one might expect if the bowel had been entered.

Illustrations of the importance of the information obtained without delay are from case records. The first four represent serious visceral injury without visible evidence of trauma to the abdominal wall.

C. A. (No. 42-3960), a 41-year-old woman, was driving her car when it was struck and overturned. On admission she complained of severe pain in the chest and abdomen. The systolic blood pressure was 90, the diastolic 60. Abdominal tap revealed free blood. She was operated upon immediately. A large actively bleeding rent in the liver was repaired.

In this instance there was doubt as to whether the primary injury was in the abdomen or in the thorax with referred abdominal pain. This question was readily answered.

J. P. (No. 42-4922), a 50-year-old man, was struck by an automobile. On admission he was in shock, unconscious, with bruises and abrasions over the head and extremities and a compound fracture of the right forearm. He improved but slightly after administration of plasma. Because of the sustained shock internal bleeding was suspected. Abdominal puncture was productive of frank blood. Operation revealed an extensive laceration of the mesentery.

In the absence of symptoms or signs a certain diagnosis of internal bleeding was made in an unconscious patient.

S. P. (No. 13821), a 32-year-old man, fell off a motor scooter at an amusement park. He had considerable pain in the left lower chest but his general condition was good. He showed no clinical evidence of internal hemorrhage until twelve hours later when he began to perspire and felt weak. Abdominal puncture in the left flank revealed blood, and a ruptured spleen was removed.

J. T. (No. 42-8973), a 71-year-old man, was knocked down by a truck. He was admitted complaining of severe pain in the abdomen. There was definite rigidity but no marks of trauma. A peritoneal tap was done and turbid yellow fluid was aspirated. Smears showed a few leucocytes and many bacteria. Immediate exploration disclosed a perforation of the sigmoid colon.

It is not always easy to tell whether visceral perforation or hemorrhage is present, but in the previous case the differential diagnosis was greatly simplified.

Not infrequently puzzling situations arise where there is not only a question as to the correct diagnosis but also as to the proper management. We have been able to answer some of these questions by abdominal puncture.

E. H. (No. 9148), a 39-year-old woman, was admitted with a history of abdominal pain and vomiting for one day. Because of moderate abdominal distention and intermittent bowel sounds a diagnosis of intestinal obstruction was considered. Abdominal puncture was productive of frank blood. On closer questioning a fair history was obtained for ruptured ectopic pregnancy, which was found at operation.

B. H. (No. 42-7900), an asthenic man, 36 years old, had severe abdominal pain with radiation to the left shoulder for twelve hours before admission. There had been pain in the upper abdomen after meals for two years and weight loss for several weeks. A barium study one week before admission indicated duodenal ulcer. The abdomen was rigid. On abdominal puncture, free blood was withdrawn. Operation revealed a primary carcinoma of the left lobe of the liver which had bled spontaneously.

K. D. (No. 41-12824), an obese 40-year-old woman, was admitted complaining of severe abdominal pain for about one hour. There had been intermittent pain in the right upper quadrant for a month previous. On admission she was sweating freely and had a diffusely tender abdomen. Peritoneal aspiration produced turbid brown fluid which on microscopic examination was seen to contain cholesterol crystals. A tensely swollen acutely inflamed but unruptured gall bladder was found at operation.

A. W. (No. 42-8085), a 47-year-old woman, had a history of repeated abdominal swelling for one year with attacks of pain and vomiting characteristic of biliary colic. On admission abdominal puncture was done and fluid containing bile and cholesterol crystals was withdrawn. Because of her poor condition operation was deferred. Exploration three weeks later revealed a subhepatic collection of "white" bile and a thick-walled gall bladder containing normal appearing bile but no calculi. There was no evidence that gross perforation had occurred.

W. S. (No. 42-15010), an emaciated elderly man, suffered pain in the abdomen for four days. This had become somewhat worse on the day of admission. The right side of the abdomen was rigid and there were findings suggestive of pneumonia in the right lung. Aspiration in the right lower quadrant revealed viscid pale yellow fluid typical of that seen following perforation of a peptic ulcer. A ruptured gastric ulcer was found at operation.

P. T. (No. 41-18115), a 30-year-old woman, was shot through the abdomen. At operation extensive intestinal injury was repaired. There was a retroperitoneal hematoma on the left side but exploration of this region was not thought to be justified. Five days later abdominal swelling developed to the left of the midline. Aspiration yielded blood-tinged fluid which was unmistakably urine.

DISCUSSION

These few cases are briefly reported to indicate some of the uses of this simple procedure. It should be emphasized that it is only an aid in diagnosis and should be interpreted as a part of the clinical examination. Positive data are significant but "dry" taps must usually be considered as meaningless. It is often repeated in such instances. If sufficient indications for operation are present a negative tap should be disregarded.

We have no accurate figures as to the frequency with which abdominal puncture is done but a conservative estimate would be over one hundred times a year, enough so that we consider it almost a routine

procedure. We believe it should be employed in any case in which fluid of any type is suspected even if not clinically demonstrable. In known or suspected nonpenetrating abdominal trauma the examination is not considered complete without a tap. The finding of free blood has led to the removal of several ruptured spleens at an early hour, which otherwise possibly would have been recorded as delayed rupture, and with a definitely higher mortality rate.

It is particularly of value in cases where the diagnosis is in doubt and where time is a factor. Thus, if blood is obtained from the abdominal cavity, other time-consuming procedures such as hematocrit or specific gravity determinations to differentiate shock from hemorrhage may be eliminated. Furthermore, we have found that a sample of aspirated fluid may convince the patient as well as the surgeon of the necessity for immediate operation. It is so strikingly enlightening at times that one might paraphrase Deaver's aphorism about the scalpel and say "the aseptic needle dispels the mystery and reveals the truth."

SUMMARY

Diagnostic abdominal puncture is a safe, simple, and often valuable procedure, particularly for the rapid appraisal of nonpenetrating abdominal injuries as well as other acute surgical conditions within the peritoneal cavity. Several illustrative cases are cited.

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THE INFLUENCE OF DUODENAL CONTENTS ON INTRAGASTRIC ACIDITY

An Experimental Study*

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THE view that duodenal regurgitation is essential or important for the reduction of gastric acidity has been presented by Boldyreff[4, 5] and others.[1, 2, 6, 10, 20, 22, 25, 27] MacLean and Griffiths and others[3, 9, 13, 21] have opposed this view and have held that duodenal regurgitation is not an important factor in the reduction of gastric acidity.

It appears true that duodenal regurgitation is a physiologic process which occurs at variable but unpredictable intervals during the gastric cycle. There is a difference of opinion on the extent to which duodenal regurgitation normally decreases the acidity of the gastric contents. McCann[16, 17] did not find any difference of gastric acidity after draining the duodenal contents into and away from the stomach, while Wilhelmj, O'Brien, McCarthy, and Hill obtained contrary results. Wilhelmj, O'Brien, and Hill noted the reduction of acidity of whole stomach pouches when acid was introduced into them. Goldberg noted reduction of acidity of isolated stomach pouches, into which duodenal regurgitation could not occur.

The objective of the present study was to attempt to ascertain the significance of regurgitation of the duodenal contents in neutralizing intragastric acidity by drainage of the duodenal contents into the stomach.

METHOD

Two series of experiments on healthy dogs ranging in weight from 8 to 12 kg. were performed. All operative procedures were performed with the animals under ether anesthesia and aseptic technique was used. In one series, a fistula of the reverse intestinal loop type[19] was made. A loop of the distal portion of the ileum 12 cm. long with its blood supply intact was isolated, the continuity of the bowel being maintained by an end-to-end or side-to-side anastomosis. The distal end of the isolated loop was anastomosed to an opening made just proximal to the pyloric orifice and the proximal end of the loop was brought out through a stab wound to the right of the midline and anchored in

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the subcutaneous region. Two weeks later the proximal end of the loop was opened so that a gastric (pyloric) fistula resulted. Owing to the direction of peristalsis in the intestinal loop, no leakage of the gastric contents occurred.

The animals were ready for observation after healing of the wound. They were fasted for twenty-four hours before each experiment. Samples of gastric contents were withdrawn by introduction of a well-lubricated rubber catheter to a marked length, so that the tip just protruded into the stomach. This insured the withdrawal of only the gastric contents as they are about to leave the stomach. This is important, since samples of gastric juice obtained from the cardiac and the pyloric regions of the stomach show a difference of acidity.[11]

Two specimens of about 5 c.c. each were withdrawn from the stomach with the animal in the fasting state. The animal was then fed a standard meal of 200 Gm. of canned meat with 250 c.c. of water. Specimens were drawn subsequently, about 5 c.c. each, every fifteen minutes for eight hours or more. On an average, thirty specimens were collected daily from each dog, for several days, so that estimations of pH were made on 400 to 500 specimens, to serve as control for each dog.

The determination of pH was made by using Northrup's potentiometer with quinhydrone oxidation-reduction potential.

Following a period of rest of two weeks or more after the control study, the duodenum was isolated by sectioning proximally at the pyloroduodenal juncture (which point was just distal to the gastric opening of the pyloric fistula) and distally about 10 cm. beyond the duodenojejunal junction. The proximal end of the duodenum was closed by inversion of the stump. The distal end of the duodenojejunal loop was anastomosed to an opening made high in the fundic region of the stomach by an end-to-side or side-to-side anastomosis (Fig. 1). The gastrointestinal continuity was maintained by a modified type of Polya anastomosis between the cut ends of the pyloris and the jejunum. Particular care was taken to prevent excision of any part of the gastrointestinal tract, in order to insure as much physiologic integrity as possible.

The studies were not begun until after complete recovery of the animal, as evidenced by its regaining a normal appetite and normal weight. The specimens were then collected, as in the control procedures, from the stomach in the fasting state and every fifteen minutes from the stomach during digestion, for eight hours or more after the feeding. As in the controls, determinations of pH were made on 400 to 500 specimens, after the duodenal contents had been drained into the stomach. (To avoid frequent repetition of a lengthy phrase, the term "duodenal drainage" is used in this communication to indicate the drainage of duodenal contents into the fundic region of the stomach.)

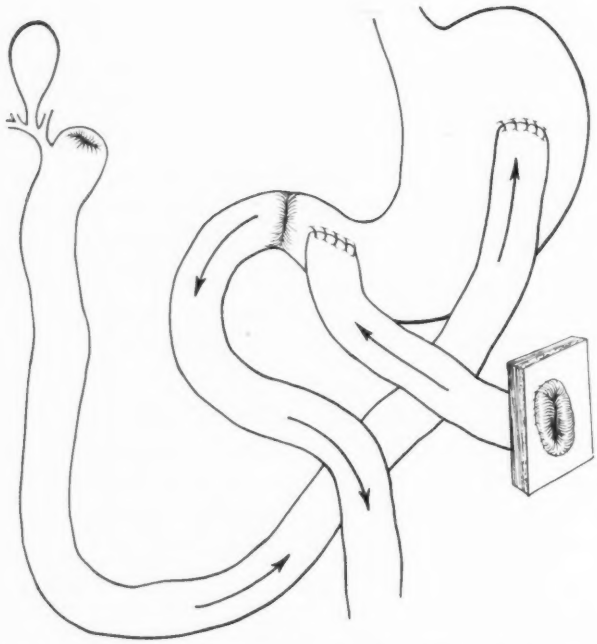

Fig. 1.—Drainage of duodenal contents into fundic region of stomach with reverse intestinal loop fistula in pyloric region.

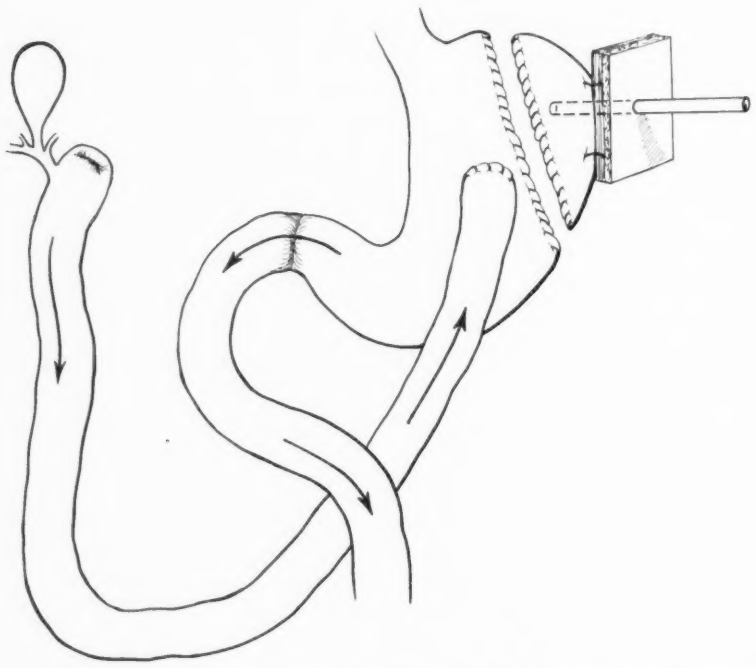

Fig. 2.—Drainage of duodenal contents into fundic region of stomach after an isolated fundic pouch has been made.

In the second series of experiments we made an isolated fundic pouch, which was drained externally by a self-retaining soft rubber catheter brought out through a left subcostal stab wound (Fig. 2).

After recovery, the secretions of the entire pouch were collected at three, six, and twenty-four hours after each meal. The dog was fasted for twenty-four hours before the standard meal was given. The quantity, pH, and free and total acidity of all the samples were determined. Free acidity was determined by titration with one-tenth normal solution of sodium hydroxide. Töpfer's reagent being used as the indicator, and the total acidity by continuing the titration with phenolphthalein as the indicator. The titration values are expressed as clinical units.

Control readings were obtained for several weeks and then the duodenum was drained into the upper part of the fundic region of the stomach, as previously described. After recovery of the animal, the studies were continued exactly similarly to those of the control series.

RESULTS

Complete studies were obtained on five dogs that had a pyloric fistula and on three dogs that had a fundic pouch. In all eight cases the internal duodenal drainage into the fundic region of the stomach was successfully performed.

A. *Internal Duodenal Drainage Into the Stomachs of Dogs That Had a Pyloric Fistula.*—We obtained several hundred determinations of pH of specimens collected every fifteen minutes, before and after duodenal drainage.

Gastric acidity in the fasting state: The control studied showed that the secretion in the resting stomach was clear and of small quantity, was often intimately mixed with abundant mucoid secretion, rarely contained any bile, and was of moderate acidity or very infrequently neutral or slightly alkaline. The presence of mucous did not appear to alter the acidity of the gastric contents materially, although when the secretion was extremely scanty and viscid, acidity was low. The acidity was not any lower than usual when bile-stained fluid was obtained, as infrequently occurred.

After duodenal drainage, the volume of the contents of the resting stomach was definitely increased. Every specimen was invariably bile-stained, which was considered as proof of the patency of the anastomosis between the duodenojejunum and the stomach. In spite of the minimal secretion of acid of the resting stomach and the presence of the alkaline duodenal contents which are being constantly secreted and evacuated into the stomach, it is noteworthy that the acidity of the fasting stomach was not reduced to any marked extent.

Gastric acidity during digestion: During the eight-hour periods of observation after feeding, a comparative study of the gastric acidity before and after drainage of the entire duodenal contents into the

stomach showed that there was not a marked reduction of gastric acidity. In two dogs higher levels of acid were obtained after duodenal drainage than before, while in three animals the maximal level of acid after duodenal drainage was slightly lower than the control values. The minimal level of acid of the gastric contents after duodenal drainage was higher in three dogs and lower in two dogs than the control values. All the samples were intensely bile-tinged and showed the presence of bile by the usual chemical tests. There was a tendency for the stomach to evacuate more rapidly after duodenal drainage than in the controls. There was no extreme variation of acidity of the gastric contents after duodenal drainage as in the controls, moderately high acidity within narrow ranges being maintained (Fig. 3 and Tables I and II).

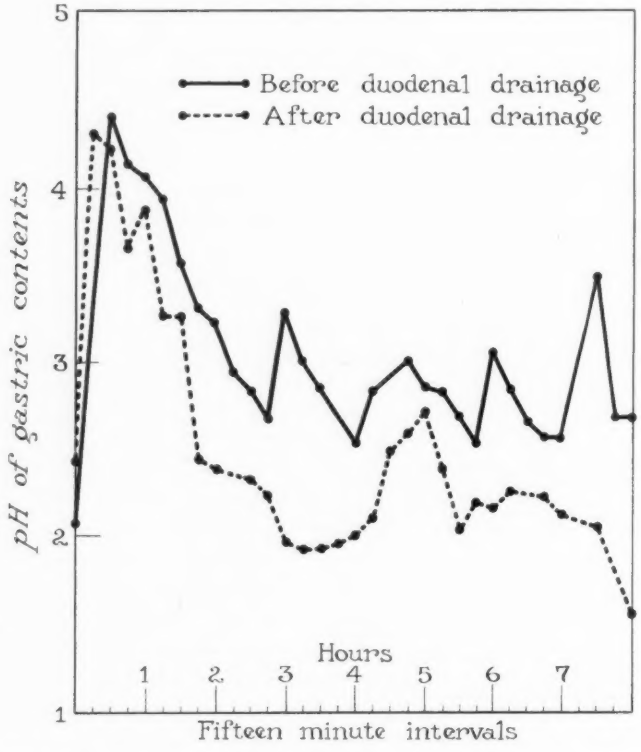

Fig. 3.—Showing pH of gastric contents before and after duodenal drainage into the stomach.

B. *Internal Duodenal Drainage Into the Stomach of Dogs That Had an Isolated Fundic Pouch.*—The quantity of secretion of three-, six-, and twenty-four-hour specimens from the fundic pouches was definitely greater in all three dogs after duodenal drainage than in the control period. In one dog the total secretion for twenty-four hours after duodenal drainage was twice, and on some days even three or four times, the secretion before duodenal drainage. In all the dogs that had iso-

TABLE I

pH OF GASTRIC CONTENTS

TYPICAL pH VALUES BEFORE AND AFTER DUODENAL DRAINAGE, FROM FIVE DOGS THAT HAD PYLORIC FISTULAS

TIME AFTER FEEDING (HR.)	CONTROLS					AFTER DUODENAL DRAINAGE				
	DOG 1 3/7/40	DOG 2 12/13/39	DOG 3 5/24/40	DOG 4 3/23/40	DOG 5 12/19/39	DOG 1 9/16/40	DOG 2 3/21/40	DOG 3 10/23/40	DOG 4 6/14/40	DOG 5 4/24/40
Fasting	5.56	6.12	6.97	6.91	4.47	2.41	4.95	5.10	4.32	1.73
1	3.76	2.65	3.87	3.49	3.38	3.88	2.71	3.85	4.35	4.63
2	3.21	2.19	3.90	4.83	2.38	2.39	2.71	3.27	4.05	3.70
3	2.81	2.26		4.83	2.33	1.97	2.23	3.05	3.73	1.78
4	3.43	2.58	3.71	4.26	1.97	2.00	2.49	3.15	3.48	1.32
5	3.69	2.71	2.95	3.35	1.95	2.70	2.31	3.32	3.24	1.44
6	2.18	2.22	3.30	2.07	1.80	2.17	1.85	3.48	2.81	1.34
7	2.12	2.07	2.87	2.07	1.93	2.12	1.99	3.09	2.05	1.44
8	2.09	2.26	3.10	2.62	1.85	1.56	1.92	2.73	1.95	1.52

TABLE II

pH RECORD*

DOG	GASTRIC CONTENTS IN FASTING STATE				GASTRIC CONTENTS DURING EIGHT HOURS AFTER FEEDING			
	CONTROL		AFTER DUODENAL DRAINAGE		CONTROL		AFTER DUODENAL DRAINAGE	
	LOWEST PH	HIGHEST PH	LOWEST PH	HIGHEST PH	LOWEST PH	HIGHEST PH	LOWEST PH	HIGHEST PH
1	1.52	6.65	1.53	3.17	1.66	5.67	1.48	5.52
2	1.47	6.49	1.88	6.29	1.54	3.11	1.83	3.97
3	2.32	7.63	2.95	6.32	1.97	6.68	2.59	4.39
4	3.33	6.91	3.05	5.20	1.81	5.52	1.89	5.32
5	1.88	4.47	1.65	3.71	1.48	3.28	1.32	4.63

*Lowest and highest in all the dogs of this series (that had pyloric fistula) during the entire period of study, before and after duodenal drainage.

TABLE III

SECRETION OF ISOLATED FUNDIC POUCH BEFORE AND AFTER DUODENAL DRAINAGE*

AVERAGE FOR TWO WEEKS	DOG	3 HOURS			6 HOURS			24 HOURS			TOTAL QUANTITY FOR 24 HOURS (C.C.)
		QUANTITY (C.C.)	FREE ACID	TOTAL ACID	QUANTITY (C.C.)	FREE ACID	TOTAL ACID	QUANTITY (C.C.)	FREE ACID	TOTAL ACID	
Control	6	27	112	120	23	150	158	42	104	108	92
	7	26	129	136	65	156	160	98	140	146	189
	8	51	153	160	58	150	162	34	73	81	143
After duodenal drainage	6	35	152	158	28	152	160	54	110	116	117
	7	44	160	167	83	157	161	170	153	160	297
	8	71	155	165	73	161	168	174	142	151	318

*Typical average values from three dogs.

lated fundic pouches the free and total acidities in three- and twenty-four-hour secretions of the pouch were definitely higher after duodenal drainage than before. The maximal acid levels, as determined by pH, were higher after duodenal drainage than those of the controls. The conspicuous feature was the qualitative (acid) and quantitative augmentation of the secretion of the pouch, which was long sustained after duodenal drainage. In the control experiments, there was a tendency of the gastric acidity to reach a very low level in the twenty-four-hour specimens, whereas after duodenal drainage, the acidity was maintained at a high level. This augmented and long-sustained gastric acidity, as measured by the miniature stomach, would appear to have been due to the presence of the duodenal contents in the stomach or the lack of them in the intestine (Fig. 4 and Table III).

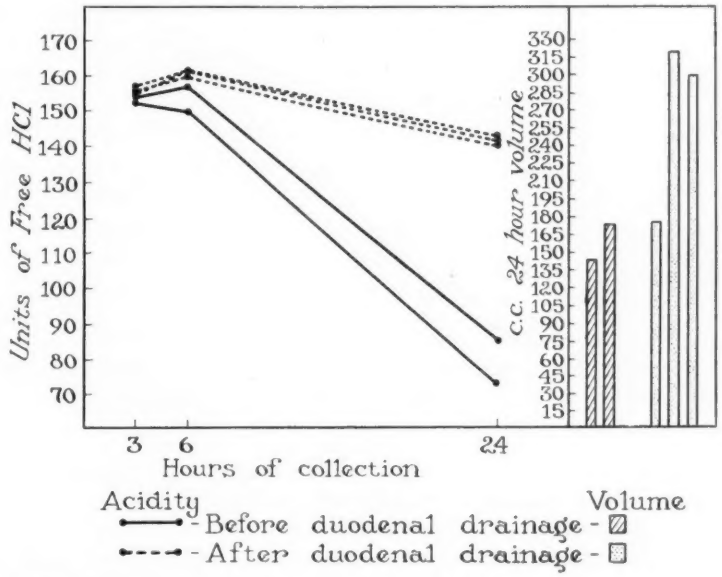

Fig. 4.—Free acidity of secretion of fundic pouch before and after duodenal drainage into the stomach. Each curve is an average for two weeks.

COMMENT AND SUMMARY

An attempt has been made to evaluate the neutralizing capacity of the duodenal contents on the acidity of the gastric contents, with a view to ascertain the role played by duodenal regurgitation in controlling gastric acidity under physiologic conditions.

Two groups of dogs were chosen for study. One group had gastric (pyloric) fistulas and the other had isolated fundic pouches. The duodenum was short-circuited into the fundic region of the stomach in both groups of dogs so that all the duodenal contents passed into the stomach. No attempt was made to determine if the quantity and quality of the duodenal contents were normal under the conditions of the experiments.

Gastric samples were collected from the first group of animals through the pyloric fistula every fifteen minutes for eight hours or more while the animals were fasting and after feeding, and the pH of the samples was determined electrometrically.

The secretion from the fundic pouch in the second group of animals was collected three, six, and twenty-four hours after feeding, the quantity was noted, and the free and total acidities were determined titrimetrically.

The results showed that duodenal regurgitation into the stomach, as determined by the presence of visible bile, occurs infrequently in the fasting state as well as during digestion. Its presence was not associated, however, with alterations of the acidity curve of the gastric contents.

After the entire duodenal contents had been diverted into the stomach, some dogs that had pyloric fistulas showed an increase of gastric acidity while others showed some reduction, although not marked. The gastric evacuation time was definitely decreased after gastrojejunostomy (modified Polya), which was a part of the operative procedure in duodenal drainage. This, in itself, might have contributed in no less degree to the reduction of gastric acidity noted in some animals (Wangensteen and co-workers). Effective neutralization or inhibition of the acid secretion never occurred.

In the dogs that had isolated fundic pouches, short-circuiting of the duodenal contents into the stomach was followed by an increase of the quantity and the acidity of the gastric secretion.[24] This result is similar to the augmented gastric secretion that occurs when alkalies are administered orally.[8, 14, 15, 24]

The results of these experiments would appear to demonstrate that the presence of even the entire duodenal contents in the stomach does not cause effective neutralization, buffering, and dilution of gastric acidity in either the fasting or the digesting state. It is questionable if the slight and infrequent duodenal regurgitation that occurs normally can be a primary and essential factor in controlling intragastric acidity.

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DESTRUCTIVE ANGIOCYSTIC DISEASE OF THE PANCREAS

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ARVID LINDAU, of Lund, Sweden, from a study of all cases of cerebellar cysts reported in the literature during the previous twenty years, together with sixteen of his personal cases, demonstrated, in 1926, the tendency for hemangiomatous cerebellar cysts to be hereditary and to be associated with the angiomatosis of the retina, described by von Hippel in 1904 (von Hippel's disease), as well as cystic disease of the medulla, spinal cord (syringomyelia, syringobulbia), pancreas, kidneys, liver, suprarenal glands, and epididymis. The cerebellar cysts contained angiomatous channels separated by sheets or strands of cells which Lindau termed pseudoxanthomatous. Of the associated abnormalities in the abdominal organs, cystic degeneration of the pancreas was the most frequent. The association of the angiomatous cerebellar tumors with a cystic pancreas had been noted previously by Berblinger, in 1922, and by his pupil Ledebur, in 1926.

In 1930, in a lecture given in London, Lindau said that "the cystic pancreas is, in adults, almost pathognomonic for the syndrome," but added, "these abdominal lesions associated with capillary angiomatoses are not *themselves* vascular, as far as I have observed." Putshar, in 1935, made a similar comment regarding the nonvascular nature of the visceral lesions. In a careful review of the literature it appears that angioma of the pancreas is a rare finding. Isolated cysts of the pancreas are by no means uncommon, but actual destructive cystic disease of the organ is definitely unusual. In a case reported by McKechnie and Priestley the possibility of Lindau's disease was suggested by the pathologist, but the authors were unable to confirm the diagnosis clinically.

Busni, in 1928, described what he believed to be the first recorded case of an angioma of the pancreas of arterial origin. This was studied carefully and the illustrations are convincing. He wrote that he had reviewed the Russian literature as well as the general foreign literature on both pathology and anatomy without finding any reference to a similar case. Ten years later Ranström, in 1939, reported a case of venous angioma of the pancreas and emphasized the rarity of such vascular tumors in that organ. To these cases should be added two others, those of Sajewloschin and Querneau, in which the lesions were angiomas histologically. Lymphangiomas and hemangio-endotheliomas, but without generalized cystic degeneration, also have been described. About one of four or five patients with von Hippel's dis-

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ease has been found to have cerebellar cysts, and involvement of the cerebrum also has been reported by Rochat. Cushing and Bailey believed the intracranial growths to be true tumors or hemangioblastomas of a type that exudes plasma with the formation of cysts which at times have xanthrochromic contents. The familial tendency is common and Rochat reported the appearance of the disease in three generations.

Angiomatosis retinae is bilateral in 50 per cent, leads to degenerative changes with retinal detachment and usually a secondary glaucoma. Apparently metastasis does not occur from the retinal growths, but the exudative tendencies may lead to a choroidal retinitis, frequently with complete loss of vision. Because of their peripheral position, or other cause, the retinal growths may escape observation, as in the case mentioned by Cushing, in which at least eight observers had failed on ophthalmic examination to find an angioma. Rochat believes the disease to begin in the retina as a hypertrophy of an angiomatous capillary which is followed by hyaline degeneration of the capillary walls with development of gliomatous and connective tissue and secondary detachment of the retina. These angiocystic diseases occur most commonly in patients between the ages of 10 and 30 years and are rare after 50. A coincidental hypernephroma of the kidney or von Recklinghausen's disease has been reported. The cystic involvement of the pancreas rarely is prominent, usually gives rise to no symptoms, and is discovered as an unexpected post-mortem finding, frequently so microscopic as to be revealed only on histologic study. The lesions of Lindau's disease have been designated by various descriptive terms, such as hemangioblastic cysts, angiomatosis, hemangio-endothelioma, hemangioblastoma, angiomatosis retinae, hyperplastic capillary hemangioma, cystosarcoma of the pia mater, gliosarcoma, angiosarcoma, cystic cystoglioma, angiospindle-cell sarcoma, secondary sarcoma, cysts of the kidney, pancreas, and suprarenal gland.

Because cystic angiomatous disease of the pancreas repeatedly has been associated with the vascular cerebellar cysts of Lindau and the angiomatosis of the retina of von Hippel, we have attempted to determine whether it is different from the case to be reported. In this patient the entire pancreas finally was destroyed by the progressive development of multiple cysts and vascular caverns of large size, unassociated with retinal changes, neurologic evidences of space-taking intracranial lesion, or the histology of malignant disease. The findings in the case suggest a rare destructive lesion of the pancreas differing from the small or microscopic cysts found in the organ in Lindau's or von Hippel's disease. In size and angiocystic qualities the lesions resembled the cerebellar growths described by Lindau. The pathologic process was largely a rapid proliferation of new blood vessels lined by one or more layers of flattened or cuboidal endothelial cells, with frail walls of poorly developed fibroconnective tissue and little collagen, which evidently expanded or ruptured under the influence

of the blood pressure into cystlike angiomatous caverns. From the extensive endothelial proliferation some of the older caverns apparently became blocked from the general blood stream and remained as cysts containing stagnant blood, clear or colored serum. Evidence is lacking of a familial tendency, of associated angioma of the retina, or of a tumor of the central nervous system. During four years of mild psychosis the patient was examined repeatedly in various institutions for the treatment of mental and nervous diseases, without finding evidence of a space-taking lesion within the skull. We cannot, however, exclude the presence of associated cerebellar cysts, since a post-mortem examination of the central nervous system was not permitted. The optic discs were examined by W. I. Lillie and were found normal on ophthalmoscopic examination. The cysts of the pancreas, although producing few subjective symptoms, progressed to large size and finally involved the entire pancreas so that residual portions of recognizable pancreatic tissue were found only on microscopic study and then in small areas.

Obviously, it is more than probable that some references have been overlooked in reviewing the literature and quite as possible that cases similar to the one reported here never were published. However, taking these possibilities into consideration, we have failed to find any case similar to the one here reported.

The patient, aged 54 years, a widow with three adult children, previously had been in good health. Mental depression developed in 1935. The patient had had the usual childhood diseases, and menses had been regular until the menopause four years before admission. In the same year, while in deep depression, temporary glycosuria was reported and treatment for diabetes was given, but evidence of diabetes since 1935 has not been found. During the first winter she was in the hypomanic phase, with unusual physical and mental activity, euphoria, and the like. Since this time she had had psychic depressions and elevations of mental activity, considered to be a true manic depressive psychosis, always with rather mild waves which recurred yearly between April and October. For these attacks she was treated temporarily in special hospitals. Physically and neurologically, at repeated examinations, she had been found to be normal although her weight gradually fell from 180 to 140 pounds. During an annual physical examination in 1939, a mass about 8 cm. in diameter was found in the upper right quadrant of the abdomen. The patient had noticed a mass in the right flank for about five months without symptoms except a tired, drawing sensation. Her weight was then stationary but she had a slight hypochromic anemia. Complete gastrointestinal roentgen examinations, including cholecystography, revealed no abnormality with the exception of a downward displacement of the hepatic flexure. The nonprotein nitrogen value was 109; the total protein, 584; albumin, 361; globulin, 2.23; albumin-globulin ratio, 1.6; hemoglobin, 75.6 per cent; erythrocytes, 5,240,000; leucocytes, 13,550; polymorphonuclear neutrophiles, 76; lymphocytes, 24; filaments, 74, and nonfilaments, 2. No abnormality was found in the urine but an intravenous pyelogram revealed mild hydronephrosis, with the right ureter sharply pushed over toward the midline just below the kidney. Thoracic roentgenologic study showed no metastatic tumor. Under the diagnosis of probable hypernephroma of the right kidney, the patient was referred to the Temple University Hospital for operation.

On Nov. 10, 1939, the right kidney was exposed and found ptosed but grossly normal. A decapsulation and nephropexy were performed. The patient had an uncomplicated operative convalescence and was discharged from the hospital ten days after the operation.

The patient was re-examined March 22, 1940, when she was apparently in good physical condition. In September, 1940, a globular, firm mass was discovered, measuring 6 by 3.5 cm., below and to the right of the ensiform. This evidently was the same mass that previously had been ascribed to the kidney. The liver was not palpable. Roentgen studies showed that the mass did not arise from the colon. The patient was readmitted to Temple University Hospital, Oct. 1, 1940. In appearance she was a well-nourished, middle-aged woman, rational but obviously in a state of anxiety. Coliclike abdominal pains with borborygmus had occurred recently.

The abdomen was moderately protuberant and relaxed, soft, somewhat obese, without tenderness but with hyperactive peristalsis. The tense mass could be palpated to the right of the midline in the epigastric region. The physical examination was unsatisfactory due to the mental resistance of the patient. The blood sugar value was 157 mg.; hemoglobin, 75.8 per cent; erythrocytes numbered 4,260,000, and whole blood sugar, 96. Examination of the urine gave negative results.

On Oct. 21, 1940, the nonprotein nitrogen level was 29; on Oct. 15, 109; total protein, 5.84; albumin, 361; globulin, 223; albumin-globulin ration, 1.6.

Operation was performed Oct. 3, 1940. A vertical upper right rectus incision exposed a very vascular, large, multicystic mass presenting through the gastrohepatic omentum. The omentum was incised and a second lower and deeper projecting portion of the cystic mass detected. The mass apparently arose from the head or body of the pancreas. An attempt was made to dissect the cystic mass from what was thought to be the underlying pancreas. The procedure was tedious owing to the many vessels to be divided and ligated. A thin-walled cyst ruptured, with the escape of amber-colored fluid. Needle aspiration of other cysts revealed pure blood. The application of a hemostatic forceps tore the thin wall of one of the large vascular sinuses, with profuse hemorrhage, controlled by digital pressure and additional hemostats. Further attempts to enucleate the cystic mass were followed by such massive hemorrhage from fragile, thin-walled sinuses that the pulse became nearly imperceptible, and no blood pressure was registered by the sphygmomanometer for fifteen minutes. The hemorrhage was controlled by digital pressure and gauze packing; respiratory and cardiac stimulants were given, together with glucose infusion and later 480 c.c. of citrated blood. Attempts at enucleation were abandoned. The abdomen was closed with figure-of-eight wire sutures, and one large tubular glass drain was placed over the gauze sponges to enable additional packing, should such be required.

Operative and Pathologic Findings.—A large, thin-walled, angiomatous cystic tumor of the pancreas measuring about 8 by 8 cm., containing clear amber fluid, large blood sinuses or caverns, and solid tumor masses were found, together with at least one additional cystic portion which was not explored, situated below and deep to the first mass. The specimen removed consisted of what appeared to be the wall of a small cyst measuring about 2 cm. in diameter. The fluid aspirated at operation from the hemorrhagic cyst was frankly bloody. Microscopically it contained red cells, polynuclear leucocytes, lymphocytes and monocytes in the approximate proportion found in normal blood. The outer surface was smooth, the inner surface was trabeculated, showed multiple hemorrhages, and was lined by a layer of cells which in places proliferated to form small, thin-walled blood vessels. The underlying layer consisted of thin strands of acid-staining tissue in which were few nuclei but many thin-walled vessels filled with blood. There was much interstitial hemorrhage, fibroblastic proliferation, and occasional collections

of cells with round nuclei and which stained coarse granular, resembling epithelial cells that apparently filled round spaces limited by the fibrous strands of tissue. The pathologic diagnosis was angiomatoid cyst wall.

The patient left the operating room with a blood pressure of 80 mm. systolic and 60 mm. diastolic, and a barely perceptible pulse of 140. Quantities of, at first serosanguineous, and later clear, thin, slightly turbid fluid were collected from the wound by aspiration drainage; the first day 480 c.c.; the second, 600 c.c.; the third, 660 c.c.; the fourth, 720 c.c.; the fifth, 1,020 c.c.; the sixth, 960 c.c.; the seventh, 990 c.c.; the eighth, 1,200 c.c.; the ninth, 1,140 c.c.; the tenth, 900 c.c., and the eleventh 630 c.c. The drainage produced a moderate excoriation of the skin despite exposure under a bed cage and stearate of zinc dusting powder. The temperature after the second day was rarely over 99.2° F., and the pulse averaged between 90 and 100. One gauze drainage sponge was removed Oct. 9, 1940. On Oct. 10, the lamp chimney drain slipped out and that evening the last gauze sponge was removed. The patient was discharged from the hospital Nov. 3 and died Nov. 15, 1940, after a steady downward course, with drainage of foul-smelling bloody fluid from the fistula the last few days.

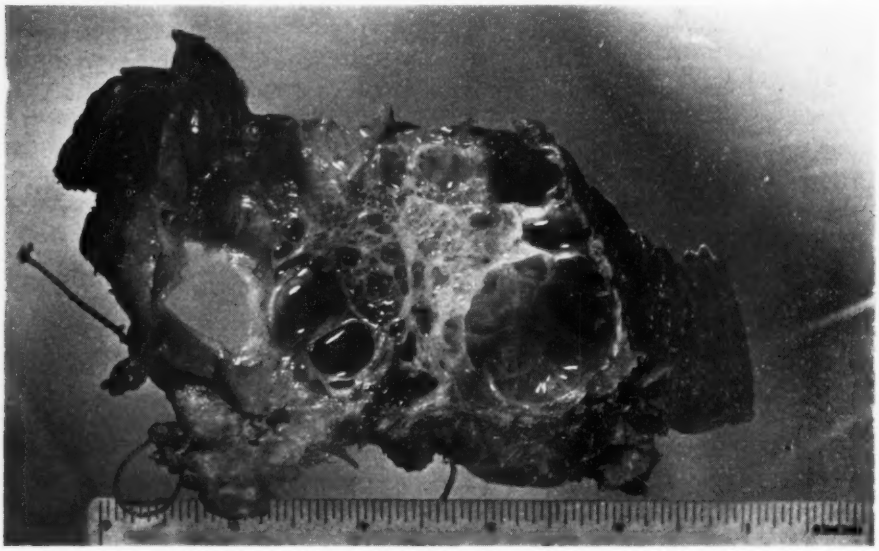

Fig. 1.—Angiocystic tumor of the pancreas with adherent portions of duodenum, removed at autopsy, showing the absence of gross pancreatic tissue and the diffuse cystic change, with clear and hemorrhagic cysts.

At an autopsy limited to the abdomen a large multicystic tumor was found located deep in the right upper quadrant and tightly surrounded by gangrenous duodenum. No grossly recognizable pancreatic tissue could be found. The base of the pancreatic fistula consisted of necrotic tissue. There were massive adhesions everywhere, some of which seemed old. There were some small, very irregular veins in the necrotic bed which had been the body of the pancreas. When the first part of the duodenum was separated from the undersurface of the liver and turned down, a second mass, approximately 10 cm. in diameter, was found in the right upper abdomen. Tightly encircling it was the remainder of the duodenum, which was black, friable, and gangrenous. It was impossible to separate the duodenum from the tumor, so they were removed together. This tumor was apparently intact, with a large vein in its pedicle.

Pathologic Report.—The cystic growth showed great structural variation in different areas (Fig. 1). In microscopic areas pancreatic acinar tissue was observed, with some distortion due to interacinar edema and the encroachment of the angiocystic disease process, but few islands of Langerhans were found (Fig. 5).

Two major pathologic processes seemed to exist side by side, or in places to merge one with the other. The first consisted of areas of cystic dilatation (Fig. 2) which honeycombed or rather replaced the pancreatic tissue and at times seemed to involve some of the secondary ducts, although the impression was gained that the process was mostly acinar in origin. The cysts were lined for the most part by flattened cells, which had moderate-sized, ovoid nuclei parallel in position to the long axis of the cell. The nuclei contained one or two rather prominent nucleoli and a moderate amount of medium-sized, deep-staining metachromatic

Fig. 2.—Thin, fragile wall of an older pancreatic cyst (×50).

granules. A gradual transition from the flattened endothelial type of cell to a frankly cuboidal cell was apparent. These cuboidal cells were vacuolated for the most part and in places showed beginning papillary proliferation and some metaplastic stratification (Fig. 2). The lumina tended to be filled with finely granular, almost homogeneous eosin-staining material. Beneath the lining of the cystic areas there was delicate connective tissue stroma in which occasional round cells were seen, chiefly lymphocytes (Fig. 3).

The other major pathologic feature was an angiomatous type of lesion (Fig. 4). The larger blood-filled cysts had walls lined by typical hyperplastic-appearing, elongated endothelial cells. In places these had proliferated to form communicating vascular channels outlined only by clumps of undifferentiated endothelial cells, which suggested a neoplastic origin. Such spaces were ill defined, sinusoidal in character, without definite intimal lining cells, as if in places, at least, due to hemorrhage. However, a definite supportive stroma of connective tissue could be identified readily in these areas when stained by Masson's trichrome stain. Running through such trabeculae, normal thin-walled, capillary vessels were identified, apparently representing the original vascular supply. Similarly, occasional

vessels with an arteriolar or even arterial musculature were seen. Occasional islands of undifferentiated cells suggested either budding new vessels or possibly pancreatic acinar formation.

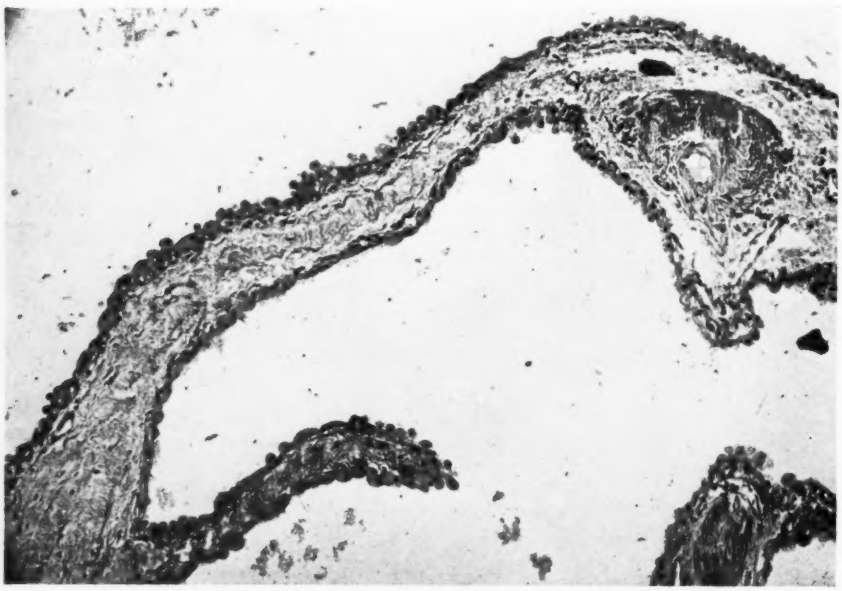

Fig. 3.—Proliferating cuboidal endothelial cells lining an older cyst (×150).

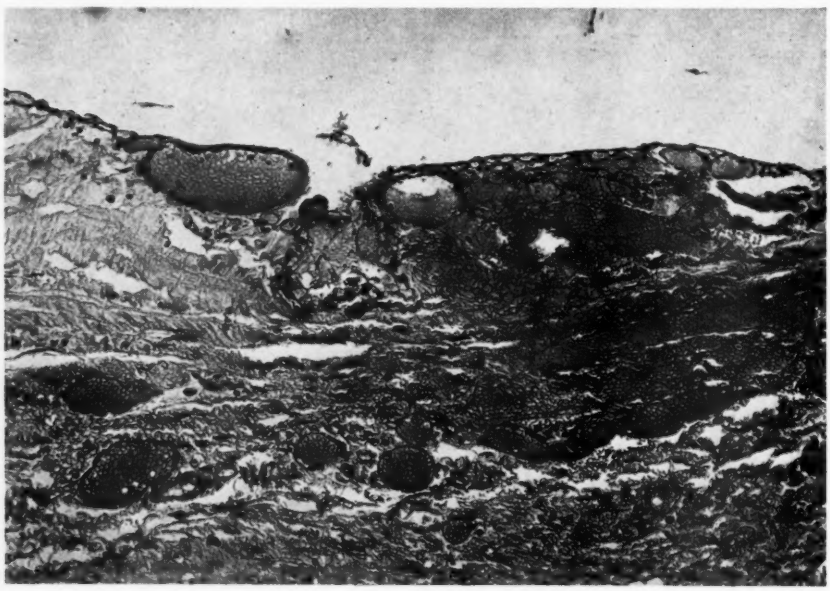

Fig. 4.—Angiomatous wall of a cyst of more recent development. (×200.)

In certain areas there was a suggestion of actual transition from the vascular pattern, with spaces filled with red cells, to the more cuboidal-like, cell-lined cyst. Even the contents of these cystic areas suggested a merging of the red cells and serouslike material.

Although the histopathology is compatible with Lindau's disease, none of the other signs and symptoms of the syndrome were evident, such as cystic tumor of the cerebellum or von Hippel's disease of the retina. Perhaps the descriptive term of destructive angiocystic disease of the pancreas conforms best to the microscopic findings of this case. It does not seem possible, however, to exclude one of the more complex mixed tumors of true endothelial origin, the so-called hemangiolymphangio-endothelioma, in our consideration of the differential diagnosis.

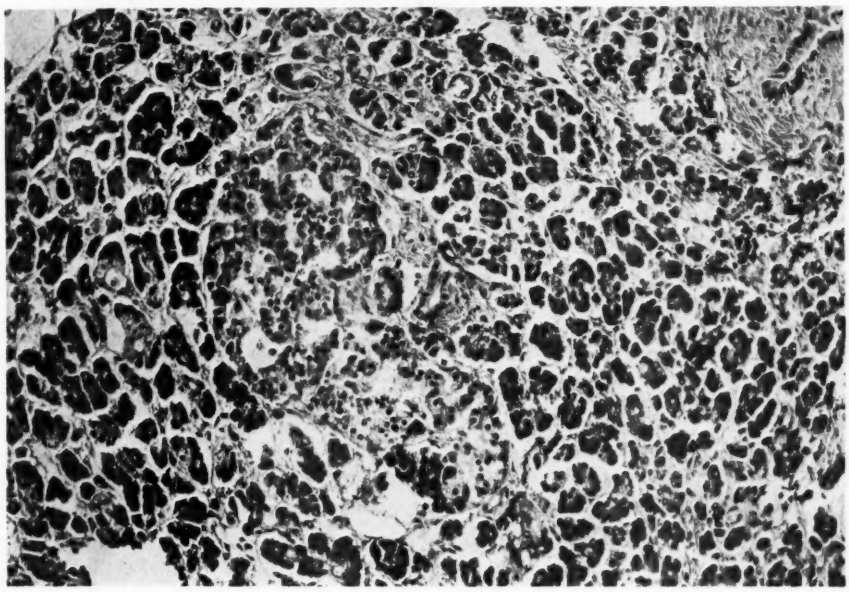

Fig. 5.—One of the few microscopic areas of persistent pancreatic tissue.

Treatment.—Our experience in this single case suggests that the chief problem in the extirpation of angiocystic disease of the pancreas is the control of hemorrhage. This may not be difficult in the early stages when the resection may be carried through the normal pancreas rather than through angiomatous tissues. Many of the cystlike cavities are great vascular caverns with very thin, fragile walls that may tear from the weight of a hemostatic forceps, with rapid loss of large quantities of blood. Additional hemostats tear larger holes in the walls, with increased hemorrhage. Even the serous cysts have walls containing innumerable vessels which on division require many fine ligatures. A coagulating current might be used for the smaller vessels but would be quite ineffective to control bleeding from the large caverns. In the early stage it would seem possible to excise the growth through the normal pancreas where blood vessels may be satisfactorily ligated and oozing controlled by sutures. For larger growths a preliminary provisional occlusion of arteries carrying blood to the pan-

creas would seem desirable when the size and vascular connections of the growth are not prohibitive.

The arteries of the pancreas are derived from the lienal for the body and tail of the organ, and from the pancreaticoduodenal branch of the hepatic artery and the inferior pancreaticoduodenal branch of the superior mesenteric artery for the head of the pancreas. In certain cases it may be feasible to do a provisional occlusion of these branches or of the hepatic, lienal, and possibly the superior mesentery trunks. A convenient method is to pass a narrow tape or soft silk ligature about each artery, the ends of which are brought through a small catheter to which they are clamped under sufficient traction to produce the desired arterial occlusion. This simple method, suggested by Astley, we have used for temporary occlusion during suture of the portal vein, the external iliac, and the common carotid artery. Obviously, very large growths and highly vascular attachments may prevent access to the supplying vascular trunks, and the growth may then be found ineradicable. Hemostasis is quite different from that found adequate in the removal of the usual large cysts of benign or malignant type which develop from the pancras. Although in the past these have been treated largely by marsupialization, increased experience has shown that removal by incising or resecting the pancreas is much less dangerous than formerly thought. As a rule it is preferable to remove these large cysts with a margin of adjacent pancreatic tissue. The pancreas is fairly firm and may be sutured or its vessels ligated. The escape of small quantities of pancreatic juice into the peritoneal cavity, when not activated by bile or gastrointestinal contents, apparently does little harm, especially when a continuous aspirating suction abdominal drain is used after the operation. When marsupialized the large cysts may become infected and discharge purulent material for many months or lead to a fistula, while an overlooked malignant process may progress and be recognized only when it has spread beyond the possibility of removal, causing the operator to regret that the original operation was not more radical. Before attempting to remove any very large angiocystic tumor of the pancreas, it is evident that the entire organ and its tributary vessels, including the pancreaticoduodenal branches of the hepatic, lienal, and superior mesenteric arteries, and the veins that run from the pancreas to the lienal and superior mesenteric veins should be investigated. If, as in the present case, the entire pancreas is involved, the outlook of course is not favorable, even with special diet and the continued used of insulin.

SUMMARY

A rare, markedly angiomatous and cystic disease of the pancreas is described which progressed to the macroscopic destruction of the entire organ, with few symptoms except a moderate leucocytosis, a rise in the nonprotein nitrogen, and an upper abdominal mass. The con-

dition apparently differs from the forms of cysts and angiomatous disease of the pancreas previously described by Lindau and others. As a nearly fatal hemorrhage followed cautious attempts to enucleate the cystic area, the desirability of early operation before the pancreas has been extensively destroyed and the use of provisional temporary occlusion of the main pancreatic arterial trunks is suggested in similar cases.

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THE ASSOCIATION OF CARCINOMA IN THE BODY AND TAIL OF THE PANCREAS WITH MULTIPLE VENOUS THROMBI

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INTRODUCTION

IN 1938, Sproul[6] first pointed out the remarkably frequent association of carcinoma in the body and tail of the pancreas with multiple venous thrombi. I have had the opportunity to examine at autopsy two cases with carcinoma of the pancreas (one in the body and one in the tail), in which the presenting symptoms and signs were referable to multiple venous thrombi. A report of these two cases, together with a full analysis of the association of phlebothrombosis with disease of the pancreas, forms the basis of this communication. Inasmuch as the physical signs of multiple venous thrombosis may be the earliest clinical manifestation of the presence of a carcinoma in the body or tail of the pancreas, it is hoped that this paper may focus the attention of clinicians on the phenomenon and assist in the difficult diagnosis of these tumors.

A correct and early diagnosis of carcinoma of the body and tail of the pancreas is rarely made. The symptoms and signs—abdominal pain, loss of weight, ascites, hematemesis, enlargement of the liver and spleen, and terminal jaundice—are not sufficiently characteristic to establish the diagnosis. Thus, in the series studied by Ransom,[5] carcinoma of the body or tail of the pancreas was unsuspected before death or operation in eleven out of sixteen. In the sixteen cases investigated by Duff,[1] not a single correct diagnosis was made despite an opportunity to examine the peritoneal cavity visually at laparotomy in four cases. The most common erroneous diagnosis in both series was carcinoma of the colon.

To avoid any misconception of the term "multiple venous thrombi" as used in this paper, it may be pointed out that the veins involved are the subclavian, the great saphenous, the iliacs, the inferior vena cava, the splenic, the portal, the inferior and superior mesenterics, etc. The thrombi usually extend throughout the entire length of these veins, with no tendency to end at a junction of two veins. Hence, the process is unique in its multiplicity and in its extent.

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CASE REPORTS

CASE 1 (Hospital No. Medicine 89906).—A 51-year-old white man was admitted to the Barnes Hospital, on June 3, 1941, and died July 17, 1941.

Illness Upon Admission.—On returning from a fishing trip in Florida in March, 1941 (3 months before admission), he noticed pain in the feet and ankles. Manipulation by an osteopath and the purchase of new shoes gave no relief. The pain came gradually to involve the entire legs, and the ankles were intermittently red and swollen. The administration of sulfathiazole was without benefit. Ten days before admission he began to have profuse night sweats and the left arm became swollen and tender. There was paresthesia in the left arm. In the preceding two weeks there were four attacks of "pleurisy." For the first time, the stools were observed to be light in color two days before entry to the hospital.

Past History.—Aside from "indigestion" he had been in good condition until this illness. As a child he had had measles and whooping cough, and in 1906, and again in 1907, pneumonia and pleurisy.

Family History.—His mother died at the age of 70 of cancer of the stomach, and one brother died at the age of 61 from "intestinal trouble, gall bladder disease, and thrombophlebitis."

Physical Examination.—Temperature, 37.3° C.; pulse, 86; respirations, 20. Examination revealed a well-developed and well-nourished man who did not appear acutely ill. Examination of the head and neck showed nothing remarkable. Auscultation and percussion of the lungs and heart revealed no abnormal findings. The edge of the liver extended 6 cm. below the right costal margin in the mid-clavicular line and was tender. There were no other palpable masses in the abdomen. Both ankles were swollen, red, and hot. Cords, presumably thrombosed veins, could be palpated in the subcutaneous tissues of the ankle and upward to the middle third of the thighs. The left arm was swollen, tender, and warm, and similar cords were palpable.

Laboratory Examination.—R.B.C., 3,620,000; hemoglobin, 68 per cent; W.B.C., 8,000; coagulation time (Howell) 33 minutes; bleeding time by the cuff method, 6 minutes; prothrombin time by bedside method, 28 seconds (normal of 23 seconds); total plasma proteins, 4.5 Gm. with albumin of 2.9 and globulin of 2.0 Gm.; blood sugar, 77 mg.; icteric index, 13.4. The Kahn test and agglutination tests for *Eberthella typhi*, *Bacillus melitensis*, and *Pasteurella tularense* were negative. Urine, 1 plus albumin and occasional white cells in the sediment. Stool, trophozoites and cysts of Endolimax nana.

Roentgenologic Examinations.—Films of the thorax were indeterminate. Films of the sinuses showed some haziness in the left maxillary sinus.

Course.—The feet and legs were elevated. Sulfathiazole, 1 Gm. every four hours for ten days, had no effect on the symptoms and signs. The temperature rose each afternoon to 38° C. On the third day pain developed in the right hemithorax and on physical examination there were a friction rub and a few fine râles in the region of the eighth and ninth ribs at the posterior axillary line. On the fourth day three additional thrombosed veins were palpable on the inner aspect of the right thigh. Cultures of the throat revealed hemolytic streptococci, pneumococci, and *Micrococcus catarrhalis*. A blood culture showed no growth.

Two weeks after admission, examination of the blood showed: R.B.C., 4,325,000; hemoglobin, 11.3 Gm.; reticulocytes, 0.6 per cent; W.B.C., 11,900; and platelets, 449,280. The bleeding time was 5½ minutes (normal, 3 to 6 minutes). Differential count: Segmented, 54; nonsegmented, 10; mononuclears, 13; eosinophiles, 9; myelocytes, 2.

During the second and third week jaundice gradually developed; by the end of the fourth week the icteric index was 44, and at the end of the fifth week it was 60. The blood nonprotein nitrogen was 42 mg. per 100 c.c.

Artificial fever therapy, three treatments on alternate days for one-half, one, and one and one-half hours to 104° F., and two transfusions of 500 c.c. and 250 c.c. respectively, brought some improvement of the swelling and pain in the legs. Because of severe nausea and anorexia, feeding with amigen, Karo, yeast, and minerals was attempted, but had to be abandoned as the nausea and abdominal distress became more marked.

At the end of the sixth week, 4,750 c.c. of bloody fluid were removed from the peritoneal cavity. Cultures of the fluid remained sterile and microscopic examination of the sediment revealed no tumor cells.

On July 16, forty-three days after admission, the patient became weaker and lapsed into a stuporous state. Examination of the chest revealed many moist râles over both upper lung fields. The blood pressure fell to 72/54 and he died the following day, July 17.

Clinical Impression.—Migratory thrombophlebitis of the legs, left arm, and pelvis; pylephlebitis; recent infarct of intestine; pulmonary infarct, right; bronchopneumonia, bilateral; and external hemorrhoids.

Autopsy (W. U. Autopsy No. 9313).—There were 3,000 c.c. of bloody ascitic fluid. The tail of the pancreas was expanded to twice normal size by a grayish white, glossy tissue. The remainder of the pancreas was normal. The greater part of the parenchyma of the liver was replaced by metastatic tumor. Metastases were present on the inferior surface of the diaphragm, in all lobes of the lungs, and in the peripancreatic, celiac, and abdominal periaortic lymph nodes. From a point 2 cm. above the orifices of the renal veins the inferior vena cava was filled with a thrombus which extended down through the common, internal, and external iliac veins bilaterally. In addition, the splenic vein was entirely occluded by a thrombus, as were also the portal vein and its intrahepatic radicles. Several of the branches of the pulmonary artery in the lower lobes of the lungs contained emboli. There were a few infarcts in the lower lobes. The veins of the greater omentum were dilated, tortuous, and filled with thrombi. Microscopic section of the pancreatic tumor showed an adenocarcinoma.

Case 2 (Hospital No. Medicine 89921).—A 67-year-old white night watchman was admitted to the Barnes Hospital for the first time on June 3, 1941.

Illness Upon Admission.—Eight weeks before admission he suddenly developed severe pain in the lower abdomen. There was an associated nausea and a change in bowel habits—urge to defecate immediately after each meal. A roentgenologic examination of the gastrointestinal tract at the Barnard Free Skin and Cancer Hospital was entirely negative. Since the onset he had lost thirty pounds in weight. On the day of admission he noticed that the left arm was swollen, slightly painful, and blue.

Past History.—He had been in excellent health until the onset of this illness. He had had pneumonia at the age of 60, but there was no history of other serious illness or injury.

The family history was negative.

Physical Examination.—Temperature, 37.4° C.; pulse, 78; blood pressure 114/70. The left pupil was slightly smaller than the right. The teeth were carious and dirty. The heart and lungs were normal. The abdomen was soft, nontender, and no organs or masses were palpable. The prostate was enlarged to twice normal size and was firm and tender. The entire left arm was swollen, cold, and a mottled blue-red. In the left axillary and supraclavicular region there was a soft swelling.

Laboratory Examinations.—R.B.C., 4,700,00; hemoglobin, 16 Gm.; W.B.C., 15,200, differential normal. Urine, 1 plus albumin; numerous hyaline and granular casts; and 20 to 30 white cells per high power field. Stools, no occult blood and no parasites. The Kahn test was negative and the blood nonprotein nitrogen was 29 mg. per 100 c.c.

Roentgenologic Examination.—A film of the thorax showed only lengthening of the aorta.

Course.—During the fifteen days in the hospital there was a persistent diarrhea, with as many as nine stools in a day. On rest, elevation, and external heat, the swelling and cyanosis of the left arm subsided and the patient was discharged on June 18, 1941.

Second Admission.—The patient was readmitted to the Barnes Hospital on July 7, 1941. Since discharge he had observed gradual enlargement of the abdomen and the appearance of jaundice.

Physical Examination.—In contrast with the first examination, just one month previously, the patient was now markedly emaciated, dehydrated, and jaundiced. The left hand was slightly edematous and a firm cordlike structure could be palpated in the left axillary space. The veins over the left pectoral region were dilated. Over the right lower thorax there were respiratory lag, slight impairment of the percussion note, diminished breath sounds, and many fine crackling râles. Fluid was easily demonstrable in the peritoneal cavity. The veins about the umbilicus were conspicuous. The abdomen was not tender and no masses could be palpated. There was edema over the sacrum and of the lower extremities.

Laboratory Examinations.—R.B.C., 4,200,000; hemoglobin, 75 per cent; W.B.C., 16,200, differential normal; blood nonprotein nitrogen, 45 mg. per 100 c.c.; blood amylase, 12 units per 100 c.c.; and plasma proteins, 5 Gm. with 2.3 Gm. of albumin and 2.7 Gm. of globulin. Urine, 1 plus albumin; 4 plus sugar, and 1 plus acetone; urobilinogen was present in a 1:25 dilution when tested with Ehrlich's reagent.

Course.—On the second day after admission, 4,000 c.c. of yellowish brown fluid were removed from the peritoneal cavity. Examination revealed a specific gravity of 1.007, and 3,000 red blood cells and 100 white blood cells (all lymphocytes) per cm. Histologic study of the sediment for neoplastic cells was indeterminate.

Clinical Impression.—Carcinoma, probably pancreatic; questionable cirrhosis of liver; portal obstruction, probably by metastatic tumor; probable pulmonary metastases; thrombosis of the left subclavian vein; generalized arteriosclerosis; and benign prostatic hypertrophy.

Autopsy (W. U. Autopsy No. 9295).—There were 2,500 c.c. of clear yellow fluid in the peritoneal cavity. The anterior part of the body of the pancreas was large, and the cut surface revealed a hard, white, dry tissue. Distally the pancreatic duct was distended to twice normal size, and contained a viscid, light yellow fluid. The tail of the pancreas had undergone atrophy and fibrosis. Tumor tissue had extended through the walls of the splenic and portal veins, and the lumens were filled with thrombi. The hepatic artery passed through the tumor, and the lumen was obliterated by compression and by a thrombus. There was a constriction of the lower third of the common bile duct by masses of tumor and dilatation of the common and hepatic ducts proximally. Many of the intrahepatic branches of the portal vein contained thrombi. Metastases were present in the liver, all lobes of the lungs, the adrenals bilaterally, and the mesentery of the ileum. Tumor tissue was found in the peripancreatic, celiac, perirectal, and thoracic periaortic lymph nodes extending to the wall of the esophagus. Throughout the tertiary radicles of the pulmonary artery, emboli were present. In all lobes of the lungs except the middle lobe of the right lung there were infarcts. The left subclavian vein was filled with a thrombus distal to the junction with the internal jugular vein. Microscopically the tumor in the pancreas was an adenocarcinoma.

DISCUSSION

The clinical histories and examinations in these two patients were remarkably similar. Both were men in the latter half of life (51 and 67

years) who sought medical advice because of pain and swelling of one or more extremity. The second patient also complained of pain in the lower abdomen and a change in bowel habits. At no time did the first have symptoms referable to the abdominal viscera, except nausea and abdominal discomfort during the last two weeks of life. An abdominal mass was not palpable in either. Both developed terminal jaundice. Both had ascites with the accumulation of a bloody fluid. It is of interest that a brother of the first patient died of some abdominal condition with "thrombophlebitis."

The clinical history was dominated by the signs and symptoms of multiple venous thrombi.

In order to extend the work of Sproul, a review has been made of all cases of carcinoma of the pancreas, whether of the head, body, or tail, in the 9,800 autopsies, records, and slides which are on file in the department of pathology of the Washington University School of Medicine. In the 9,800 autopsies there were thirty cases of carcinoma of the head of the pancreas. Of these not one was associated with multiple venous thrombi. In five there was a single thrombosed vein. Analysis of these five instances showed that in three the wall of the vein was invaded by tumor. In the remaining two the pulmonary arteries contained emboli, which by their shape were thought to have originated in the long veins of the extremities. One of two was associated with cardiac decompensation. Therefore it is obvious that the thrombi found with carcinoma of the head of the pancreas can readily be explained by well-recognized mechanisms.

In the same series of autopsies, twenty-one cases of carcinoma of the body or tail of the pancreas were available for study. Seven, or 33.3 per cent, showed multiple venous thrombi. Ten, or 47.6 per cent, had at least one thrombus. This compares with the figures of 31 per cent and 56 per cent respectively, reported by Sproul. These figures are in marked contrast with those obtained in cases of carcinoma in the head of the pancreas.

Before any conclusions may be drawn concerning the relation of carcinoma of the body and tail of the pancreas and multiple venous thrombi, it is well to review each of the various factors which might conceivably influence the incidence of thrombosis.

Debility.—Debility is no more characteristic of carcinoma of the *body* and *tail* of the pancreas than it is of cancer of the *head* of the same organ, or no more characteristic of this condition than of any other chronic and wasting disease. Since the multiple venous thrombi are found much more frequently in the condition under discussion, debility cannot be the basis for the phenomenon.

Cardiac Decompensation.—Naturally, cardiac decompensation with venous stasis should be considered as an explanation for the clinical picture presented by these patients. In one of the seven cases revealing

multiple thrombi there was clinical evidence of cardiac failure. Digitalization had been carried out and the patient was considered clinically as compensated. Therefore, it is highly improbable that decompensation was the fundamental factor, although it may have contributed in that one case.

Mechanical Pressure.—In the cases reviewed, none that could be explained on the basis of pressure by the primary tumor or lymph nodes containing metastases was considered to represent thrombosis as discussed in this communication. The extent and positions of the thrombi rule out direct compression as a factor.

Invasion of the Vein Wall.—If invasion of the vessels by tumor is a major factor of pathogenesis, then carcinoma of the *body* and *tail* of the pancreas must be markedly different in the invasive potentialities of the cells from carcinoma of the *head* of the pancreas, and from any other malignant tumor yet known arising in any organ. Duff[1] has pointed out the greater tendency for metastasis in carcinomas of the body and tail of the pancreas, as compared with that of the head. Yet it is extremely doubtful whether sufficiently widespread dissemination of neoplastic cells could take place to produce the bizarre and widespread thrombi which occur with this condition. Direct proof that invasion of the venous wall is not the primary cause is supplied by microscopic study, which failed to reveal malignant cells at the sites of the thrombi.

"Thrombophlebitis."—Some patients who actually had carcinoma of the body or tail of the pancreas and who manifested this by multiple and migrating venous thrombosis have been designated as suffering from "migratory thrombophlebitis." It is generally agreed that infection of a vascular wall leads to clotting. Yet in the cases under consideration no infection was noted grossly, and microscopic study of the wall of the vein revealed no inflammatory process.

Disturbed Hepatic Function.—The question may be raised as to whether the role which the liver plays in blood clotting is disturbed in carcinoma of the pancreas, either by obstruction of the hepatic ducts or by destruction of the parenchyma of the liver by metastases. Of the twenty-one cases of carcinoma of the body or tail of the pancreas, only three had no metastases in the liver. These metastases were totally unrelated to the phenomenon of multiple venous thrombosis. It is, furthermore, to be noted that jaundice in these patients, if it occurred at all (five cases only), was terminal and many times not intense. On the other hand, in malignant tumors of the head of the pancreas, obstruction of the bile duct with jaundice is among the first signs. These tumors metastasize to the liver frequently enough and thrombosis is infrequent enough so that it can be stated that neither obstruction to the bile duct nor destruction of hepatic tissue is responsible for the abnormal tendency to thrombosis.

The problem is therefore reduced to the search for a disturbance in the pancreas itself as an explanation. Atrophy and fibrosis of the body and tail of the pancreas might, by reducing pancreatic tissue, remove a normal secretion and bring about an abnormal clotting mechanism. Such a pathologic change of atrophy was observed in ten out of the thirty cases of carcinoma of the head of the pancreas, yet in these cases there was no tendency to thrombosis.

Acute hemorrhagic necrosis of the pancreas damages the organ severely. Twenty-two cases of this condition were reviewed and none showed a tendency to multiple thrombosis. It is true that the veins in the immediate area of damage contained thrombi, but these were not comparable to the generalized thrombosis seen in the cases of carcinoma.

In acute interstitial pancreatitis there are edema, congestion, and infiltration with polymorphonuclear leucocytes. Eight examples of this condition were examined, with negative results.

Increase in the interlobular and intralobular fibrous tissue of the pancreas may be the result of a previous injury, of arteriosclerosis, or it may be a part of the process of ageing. In any event the function of the organ might diminish. Thirty-five patients showing these changes were chosen at random from the same general group as the previously cited instances of carcinoma of the pancreas. None showed multiple venous thrombosis, although seven had a single thrombus. All of these seven may be readily explained: two cases were caused by embolism from a mural thrombus in the heart, two by pyemia, two by cardiac decompensation, and one occurred in an immediate area of injury.

In diabetes mellitus a disturbance of pancreatic function may be postulated, with a dysfunction of at least one type of cell. Accordingly, the protocols of autopsies in twenty-seven diabetic individuals were analyzed. Eleven of these showed hyalinization of the islands of Langerhans. Not one had more than one thrombus, and only three revealed a single thrombus, the basis for each of which was clear: mural thrombus in the heart giving rise to a pulmonary embolus (two cases), and thrombosis of the left femoral and iliac vein following an amputation of the left leg (one case). Furthermore, consideration of such relatively uncommon processes as adenoma of the pancreas (four cases), hemochromatosis of the pancreas (four cases), tuberculosis (one case), and advanced chronic passive congestion of the pancreas (four cases), shows that none of them was associated with thrombosis.

In the group of metastatic tumors destroying the pancreas, leucemic infiltrations are included. Forty-one examples were reviewed and two were found to have multiple venous thrombi without any satisfactory explanation. Both of these were instances of carcinoma of the stomach, and Sproul has pointed out that this tumor is third in the series of carcinomas associated with multiple venous thrombi. Six of this group

showed a single thrombus. Three of these were caused by direct invasion, one by compression, and two were unexplained.

It is clear that only in the case of a primary carcinoma of the pancreas located in the *body or tail* is there a consistent development of multiple venous thrombosis. It appears to be a peculiarity of these tumors that the blood clotting mechanism is disturbed in this way. Either the neoplasms secrete an excessive amount of a substance normally produced by the pancreas and involved in the clotting of blood, or they give rise to an abnormal substance which hastens clotting. Sproul has made several suggestions as to how the clotting mechanism may be disturbed.

The microscopic appearance of the tumors of the body and tail was studied and it was found that thirteen contained mucinous foci. All examples of multiple thrombi fall within this group. Sproul noted that all except one of her patients with multiple thrombi had mucinous foci. Inasmuch as some tumors contained mucin and were not associated with thrombi, Sproul felt that no causal relation could be expressed. Nevertheless, it is striking that no tumor without mucin shows the phenomenon. Of the thirteen cases showing mucin, seven had multiple thrombi. In two, autopsy permission was limited to an examination of the abdominal cavity, and no statement could be made regarding the condition of the veins. In one there is some question as to whether the tumor arose in the head or body. Under a favorable interpretation, therefore, only three out of the thirteen cases showed mucin and no thrombi. Whichever view is taken it can be said that the phenomenon of multiple thrombosis occurs exclusively within the group of mucinous carcinomas. This lends support to the idea that primary carcinomas of the *body and tail* produce an excess of a substance which enhances the clotting mechanism. Further evidence is given by the studies of Sugiura, Pack, and Stewart[7] who extracted an adenocarcinoma of the body and tail of the pancreas and compared the result with the extract of three normal pancreases. The enzymatic action of the extract on starch, casein, peptone, and esters was comparable with the normal, that is, the tumor had a physiologic resemblance to normal pancreas.

The mucinous tumors of the pancreas may arise from the ducts. Kiefer[4] states that cylindric epithelial cells are of ductal origin; Ewing[2] concurs and mentions a rare gelatinous change; Karsner[3] feels that the cylindrical cells arise from the ducts but points out the fallacy of such a morphologic comparison when dealing with malignant tumors. It is possible that the ductal epithelium, normal or neoplastic or both, elaborates and secretes a substance that is concerned with the clotting of blood.

CONCLUSIONS

Two cases of carcinoma of the pancreas, one of the body and one of the tail, are reported. In both, multiple venous thrombosis was a prominent feature of the clinical and pathological picture.

Thirty cases of carcinoma of the head, and twenty-one of the body and tail of the pancreas are reviewed. Carcinoma of the body and tail is associated with multiple venous thrombosis in a high percentage (33 per cent), whereas carcinoma of the head shows no such striking association. Considering the difficulty of performing a really complete autopsy with an adequate examination of all veins, and in view of the ease with which a past history suggestive of multiple venous thrombi may be passed over as unimportant, even such high figures may be too low.

In view of the great difficulty in making a diagnosis of carcinoma of the pancreas early enough to be of any practical aid to the patient, the value of an early diagnostic sign is obvious. It is urged, therefore, that in every patient either suspected or known to have such a tumor, all factors of the blood clotting mechanism be studied energetically. It may be that some difference not yet suspected may become apparent or a new substance be isolated. This would in turn act as a diagnostic agent in the future. Further, in any case of so-called "migratory thrombophlebitis" the possibility of the diagnosis of carcinoma of the body or tail of the pancreas must be considered.

Carcinoma of the body and tail of the pancreas is not so rare in comparison to the incidence of carcinoma of the head as one would be led to believe by many reports (twenty-one cases compared to thirty cases in a series of 9,800 autopsies).

Extrinsic factors such as debility, cardiac decompensation, mechanical pressure, invasion of the venous wall, phlebitis, and damage to the liver were considered and found to be inadequate to explain the phenomenon.

Intrinsic factors were also reviewed. These are atrophy and fibrosis of the body and tail of the pancreas, acute hemorrhagic necrosis of the pancreas, acute interstitial pancreatitis, interlobular and intralobular fibrosis, diabetes, adenoma, hemochromatosis, tuberculosis, and chronic passive congestion. None of these are any more satisfactory as an explanation than invasion of the pancreas by metastatic tumors.

It is concluded that carcinoma of the body and tail of the pancreas is unique in being associated with multiple venous thrombi, and it is suggested that these tumors may secrete an abnormal substance or an undue amount of a normal substance concerned in blood clotting. This assumption is supported by the fact that in every case showing multiple thrombi the tumor is of the mucinous type. A thorough study of all factors in the clotting mechanisms of patients with this neoplasm is urged, in the hope that a characteristic change may be discovered and used as a diagnostic method.

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LIGATION OF THE SUPERIOR MESENTERIC VEIN

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MUCH has been written on the subject of spontaneous occlusion of the superior mesenteric vessels, but discussions on the course and treatment of injuries to these vessels have been neglected. It has been an accepted fact that the spontaneous occlusion of either the superior mesenteric artery or vein carries a nearly 100 per cent mortality rate. Isolated cases have been reported where slow occlusion of the superior mesenteric artery occurred, giving time for sufficient collateral circulation to develop and maintain the viability of the intestine. I have found no report of a patient surviving after a sudden complete occlusion of the superior mesenteric vein. We recently had a patient, the victim of a gunshot wound of the abdomen, who recovered following the ligation of the superior mesenteric vein. A report of this case follows:

E. C., a 38-year-old colored man, was admitted to the Cincinnati General Hospital about thirty minutes after receiving a gunshot wound of the abdomen.

Examination revealed a well-developed and well-nourished colored man lying flat in bed. He was quite uncooperative, which made the examination difficult. Temperature was 98° F., pulse 72, respirations 18, and blood pressure 110/70. The patient's skin was warm and he showed no external evidence of shock. His head and neck showed no remarkable findings. Examination of the chest revealed no positive findings.

In the left abdominal wall 2½ cm. above and 2½ cm. lateral to the umbilicus was found a bullet wound of entrance. The abdomen was scaphoid and showed generalized tenderness and rigidity. Peristaltic sounds were absent. Liver dullness was normal.

Palpation of the back revealed the bullet to be lying just under the skin and just to the right of the midline at about the level of the fourth lumbar vertebra. There was moderate tenderness of the lower lumbar spine, but no deformity was demonstrated.

Rectal examination revealed slight relaxation of the sphincter. No tenderness or gross blood was encountered.

A neurologic examination revealed normal cranial nerves. The reflexes and motor power in the upper extremities were normal. Motor power was present in the left leg, but the patient was unable to move the right leg. Reflexes in the lower extremities were absent bilaterally. The Babinski test produced no response. A sensory examination was impossible due to lack of cooperation from the patient.

Examination of a catheterized urine sample was negative. The white blood count was 15,800.

The diagnosis was made of a gunshot wound of the abdomen and spine with probable penetration of the stomach and cauda equina injury.

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X-ray pictures of the abdomen and spine revealed no free gas under the diaphragm, and the bullet was seen just to the right of the fourth lumbar vertebra. A fracture of the right lamina of the fourth lumbar vertebra was present.

An exploratory laparotomy was done through a long right rectus incision under cyclopropane anesthesia. Only a small amount of free blood was found in the peritoneal cavity. Perforations of the anterior and posterior walls of the stomach near the lesser curvature were found and were closed with interrupted silk sutures. The abdomen was thoroughly explored and no other injuries to the hollow organs, liver, kidneys, or spleen were found. However, in the region of the pancreas and third portion of the duodenum there was a large retroperitoneal hematoma. A clot which was located on the lower border of the pancreas was removed from the bullet tract in the posterior peritoneum and rapid bleeding ensued. The third portion of the duodenum was then mobilized, and no perforation in the duodenum was found. Mobilization of the lower border of the pancreas revealed the bleeding to be venous in character and arising from the region of the superior mesenteric vessels. Temporary hemostasis was obtained by compressing the superior mesenteric vein above and below the injured site. The superior mesenteric vein was then dissected out and was carefully separated from the superior mesenteric artery coursing next to it. No injury to the artery was found. Because of the patient's poor general condition, and due to the large size of the defect in the vein, it was decided that a repair of the vessel was not advisable. The vessel was divided and doubly ligated with double medium silk ligatures.

Following the ligation several interesting changes occurred. The vein distal to the ligature, of course, became markedly dilated, and the superior mesenteric artery also seemed to dilate slightly. The muscle tone of the entire small bowel became markedly increased and peristalsis became extremely active. Subserosal petechiae appeared over the surface of the small intestine and the venous radicals in the mesentery became dilated, but no definite diffuse cyanotic color appeared in the bowel.

The peritoneal cavity was dusted with 6 Gm. of sulfanilamide powder, and the abdomen was closed with through-and-through steel wire sutures. The patient left the operating room in fair condition. The Levin tube which had been inserted into the patient's stomach preoperatively was connected to a Wangensteen suction, and the patient was given continuous nasal oxygen. The patient had received 500 c.c. of blood and 700 c.c. of saline solution intravenously during the operation.

In accord with the advice of Dr. Louis Herrmann, heparinization was begun four hours after operation, using the continuous method and administering the drug through a continuous venoclysis inserted into the saphenous vein. The patient was given 1,000 units of heparin each hour in a normal saline solution. Determinations of the clotting time, using the capillary tube method, were made every four hours until it became maintained at between ten and fifteen minutes. After the first twenty-four hours the clotting time was nicely maintained at this level, using 1,000 units of heparin each hour. The heparinization was continued for five days after the operation, during which time no clinical evidence of bleeding either internally or externally appeared. Intravenous sulfadiazine, 4 Gm., were given daily for six days and 2 Gm. a day were given for the next three days. On the fourth postoperative day peristalsis appeared and the Wangensteen suction was discontinued. The patient received a unit of plasma on the second and third days postoperatively and after heparin therapy was discontinued, he received frequent blood transfusions. The patient's fluids were maintained with intravenous saline and glucose solutions.

On the eighth day after operation the patient began vomiting, and the Wangensteen suction was again instituted. Attempts were made to discontinue the gastric suction during the next few days, but vomiting always reappeared.

On the thirteenth day after operation an upper gastrointestinal x-ray series was done, which revealed a complete obstruction of the third portion of the duodenum. This obstruction failed to respond to conservative therapy and on the sixteenth postoperative day an exploratory laparotomy was done through a right rectus incision under gas-oxygen-ether anesthesia. Exploration of the abdomen revealed numerous adhesions throughout the upper abdomen. These adhesions were extremely abundant in the region of the third portion of the duodenum and the adjacent border of the pancreas. They appeared to have arisen as a reaction to secretions from the injured pancreas. Examination of the small intestine revealed patchy cyanotic areas throughout its length, with many patches of organizing subserosal hematomas in the mesentery. The bowel wall seemed quite viable and healthy, normal in diameter, and peristalsis was present (Fig. 1). The veins in the mesentery of the small bowel and right colon seemed slightly distended. The superior and inferior pancreatoduodenal and gastric epiploic veins were quite markedly dilated. The colon appeared quite normal except for adhesions around the mid-transverse colon which were continuous with those around the pancreas.

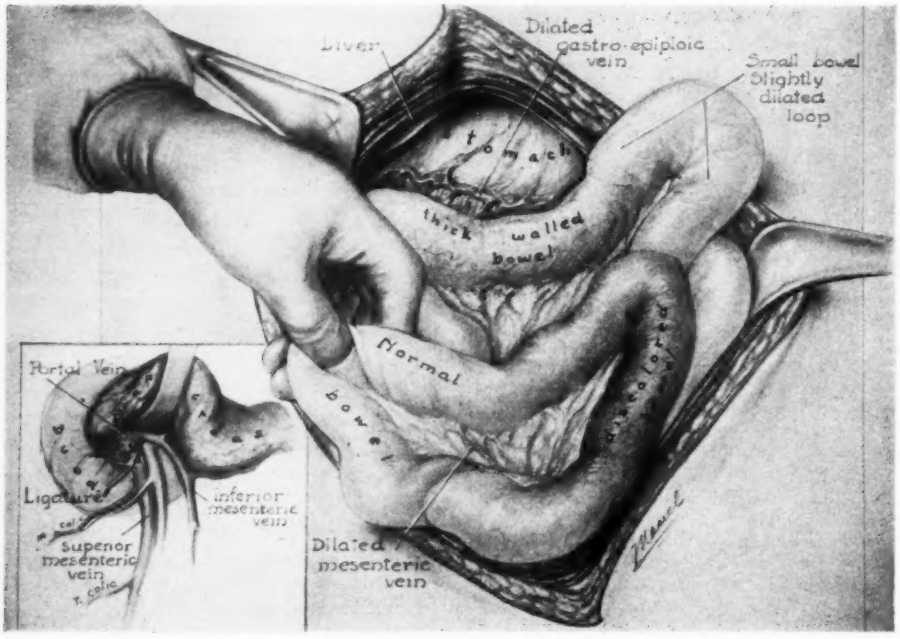

Fig. 1.—Appearance of the bowel, mesentery, and blood vessels at the time of the second operation.

An attempt was made to free the adhesions around the third portion of the duodenum and, if possible, to expose the superior mesenteric vessels in this region. Because of the abundance and density of the adhesions it was impossible to separate the scar tissue overlying these structures. It was then decided to do an anterior gastroenterostomy, using a loop of jejunum distal to the ligament of Treitz. This procedure was then done without difficulty. Sulfanilamide was placed in the peritoneal cavity and the abdomen was closed with through-and-through steel wire sutures.

Using continuous Wangensteen suction, intravenous sodium, sulfadiazine and parenteral fluids, plasma, and blood after operation, the patient continued on to a

complete recovery except for residual neurologic changes in the right lower extremity. He was discharged on his sixty-second hospital day.

He has been seen on several occasions since his discharge from the hospital. He is now on a general diet and gaining weight. He has no complaints referable to the abdomen but still does have quite marked weakness of the right leg. The abdominal wound is well healed.

The study of this case brings up for discussion several interesting practical points. The pathways through which an adequate collateral venous return was accomplished are immediately conjectured upon (Fig. 2). In 1868, Chiene[1] reported the findings of an autopsy which illustrated very nicely the collateral circulation between the visceral and parietal vessels of the abdomen. This necropsy was performed upon a patient with an aneurysm of the abdominal aorta which had, due to the formation of a laminated clot, caused the development of a complete obstruction to the celiac, superior, and inferior mesenteric arteries. It was definitely proved that the obstruction of these vessels was of long duration, and yet the blood supply of all the viscera seemed entirely adequate. With the blood vessels injected, a thorough dissection of abdominal and pelvic vessels was carried out. There had developed a good collateral circulation with the ileocolic artery through the last dorsal, lumbar, and ileolumbar vessels. A branch from the splenic artery supplied the splenic flexure of the colon, anastomosing with the arterial loop formed by the middle and left colic arteries. The superior hemorrhoidal artery was as large as the femoral and anastomosed with the ischiatic, lateral sacral, and middle hemorrhoidal arteries, all of which were dilated. It seems quite logical to assume that a collateral venous circulation may develop through the same collateral pathway by the venae comites of these arteries.

Additional collaterals between the systemic and portal circulation have been described in the standard textbooks of anatomy. Communicating veins are consistently found between the left renal vein and the middle colic veins. The left renal vein also communicates with the inferior pancreatoduodenal vein. There are connecting veins between the retroperitoneal branches of the inferior vena cava and the mesenteric veins of the intestine, the so-called veins of Retzius.

It was definitely noted in our patient at the time of the second operation that the superior and inferior pancreatoduodenal and gastric epiploic veins were definitely dilated. The superior mesenteric vein had been ligated above the origin of the inferior pancreatoduodenal vein, thus allowing a collateral venous return from the proximal portion of the small intestine to pass through the inferior and superior pancreatoduodenal veins to the gastroepiploic and thence to the superior mesenteric vein above the point of injury. The transverse colon was involved in a mass of adhesions so that the middle and left colic veins in that region could not be visualized, but, undoubtedly, the anastomosis be-

tween these two vessels must account for some of the venous flow from the right and transverse colon. The ileocolic vessels were not exposed, but a collateral could be developed between this vessel, the last dorsal, lumbar, and ileolumbar veins. The veins of Retzius may be added to this collateral venous system.

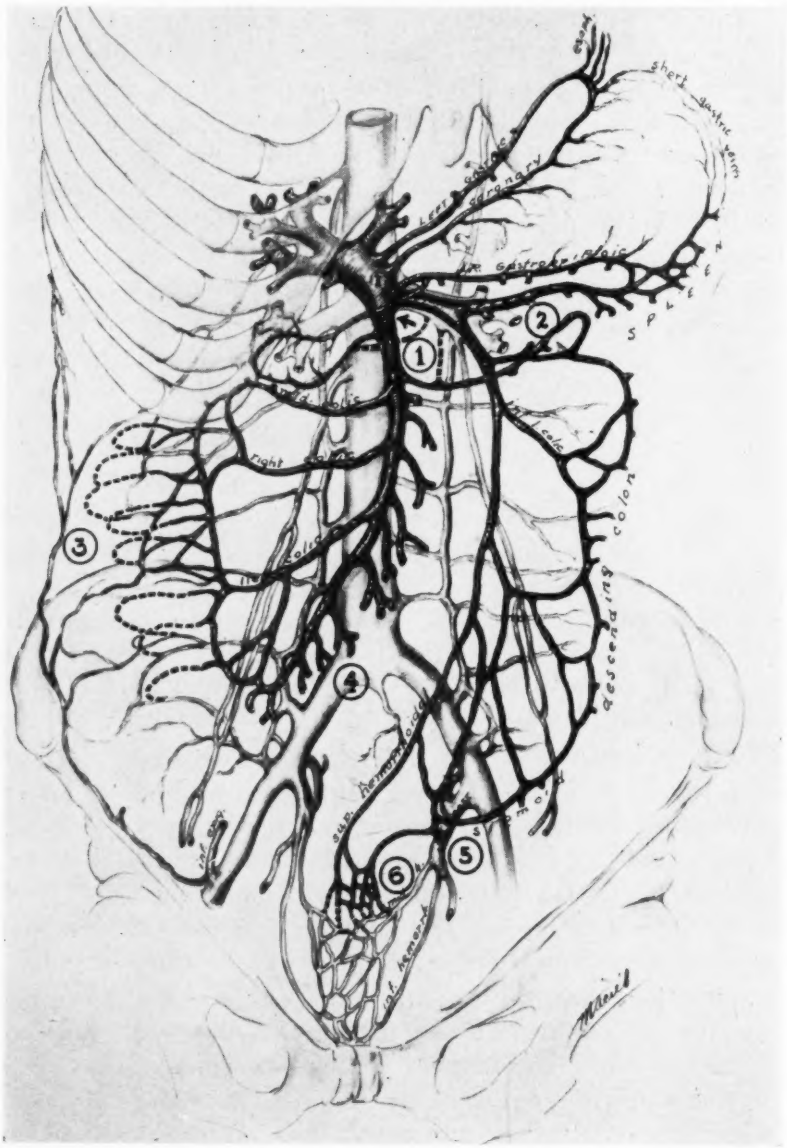

Fig. 2.—Arrow indicates point of ligation of superior mesenteric vein. *1*, Anastomoses between superior and inferior pancreatoduodenal veins, also between inferior pancreatoduodenal and left renal veins. *2*, Anastomoses between superior and inferior mesenteric veins through middle and left colic veins, also between middle colic and left renal veins. *3*, Anastomoses between ileocolic and right colic veins, and ileolumbar and last dorsal veins. *4*, Anastomoses at base of mesentery between superior mesenteric and inferior vena cava through the veins of Retzius. *5*, Anastomoses between the sigmoid and hypogastric vein. *6*, Communications between the superior and middle hemorrhoidal veins.

This patient was given continuous heparin therapy beginning four hours after operation and continuing for five days. This therapy undoubtedly played an important role in the re-establishment of the mesenteric venous circulation. Murray[2] and Laufman[3] have done experimental work in regard to the use of heparin in patients with mesenteric thrombosis. Both agree that heparinization tends to prevent the spread of the thrombotic process. Laufman believes that in cases of extensive infarction (over 5 to 10 cm.) heparin is harmful in that it promotes extravasation of blood into the wall and lumen of the bowel and thus produces shock and death. He does advise its use in conjunction with resection when only short segments of bowel are involved. We feel that in cases of extensive involvement, as well as in the less severe cases, heparinization may be of definite benefit. If given early, heparin keeps the stagnant blood in the venous channels in a fluid state, giving time for the collateral channels to dilate and develop sufficiently to take over the return venous flow. If the veins within the bowel wall and the mesentery are allowed to thrombose, then the development of collateral circulation is, of course, impossible.

In any patient with impaired circulation of a part, it is extremely important to maintain a normal blood pressure, normal blood volume, and normal oxygenation of the blood. Special attention was given to these factors in this patient's treatment. This patient's blood volume and blood pressure, in spite of severe bleeding, was maintained during and after operation by intravenous fluids, blood, and plasma. In addition, he was given continuous oropharyngeal oxygen after operation. In any patient where the development of an adequate collateral circulation is necessary to maintain the viability of a tissue, the maintenance of adequate blood pressure, blood volume, and normal oxygenation is of vital importance.

COMMENT

In studying this case, one immediately suspects that this patient may have an accessory superior mesenteric vein which took over the venous return from the small bowel. This is certainly possible, although we believe it to be quite improbable. It was noted at the operating table that, after the ligation of the superior mesenteric vein, the small intestine developed a toniclike contraction of the muscles in the bowel wall. This I have observed in dogs following the ligation of the mesenteric vein. The mesenteric veins became dilated, and subserosal petechiae appeared almost immediately. At the second operation, residual organizing subserosal hematoma were still present and the bowel wall still retained a cyanotic color in several scattered areas. This patient had an extensive injury of the vein with much destruction of vein wall which made it impossible to repair the vessel. In cases where a repair of the vessel is possible, it is probably the procedure of choice.

CONCLUSIONS

1. A case report and discussion of a patient who survived following the ligation of the superior mesenteric vein has been recorded.

2. In patients with spontaneous occlusion of the superior mesenteric vein the mortaility rate closely approaches 100 per cent.

3. The potential pathways for the development of collateral circulation incident to complete obstruction of the superior mesenteric vein were reviewed.

4. The importance of early, adequate, and continuous heparinization as an aid to the development of collateral venous channels is stressed.

5. The development of an extensive collateral circulation requires the maintenance of adequate blood pressure, blood volume, and normal oxygenization of the blood.

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THE TREATMENT OF ACUTE EMPYEMA BY CONTINUOUS TIDAL IRRIGATION*

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BECAUSE of its frequency, empyema thoracis is the most important surgical lesion of the pleura. The nature of the lesion was recognized by Hippocrates, who advocated treatment by drainage. The treatment is complicated by one's inability to put the part to rest and by the property of the lung of collapsing and creating a large cavity or dead space. To effect a cure the attendant infection must be arrested, all foreign material removed, and the dead space obliterated.

The principles underlying the mechanics of respiration should be understood by the surgeon treating this disease, and he should appreciate the possible disastrous consequences of an untimely opening of the thoracic cavity to communicate freely with the outside.

The aim of the treatment of acute empyema is twofold: preservation of the life and the prevention of the development of a chronic disease. This aim is realized by the proper application of any procedure which will give early, free, and efficient drainage to the cavity, prevent paradoxical respiratory movements of the mediastinal structures, and allow the lung to re-expand to fill the cavity and obliterate the dead space. If a dependent outlet is provided, good drainage results. Resection of the proper rib will allow effective drainage, but this procedure has some disadvantages, especially in children. A simple tube introduced between the ribs does not permit adequate drainage. A tube can be placed through the chest wall at the lowermost level of the cavity, but unfortunately the material to be removed must find an exit through an opening in the tube. This opening cannot rest in the most dependent portion of a pleural cavity and remain patent for any length of time. The pus and secretions can, however, be effectively removed through a tube if they are diluted and flushed away.

Numerous schemes[1-5] have been devised to provide continuous irrigation of empyema cavities. Hart[3-5] obtained good immediate and late results by employing tidal irrigation. The main difficulty with most of these procedures arises from the complicated apparatus used. A scheme for tidal drainage is presented in this communication, for which the apparatus is felt to be simple. If the principles governing

*The major portion of this work was done in the Lane Hospital of the Stanford University School of Medicine and the Hospital for Women and Children, San Francisco, Calif.

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the action of this device are understood, the details of its operation become self-evident.

Paradoxical respiratory movements of the mediastinal structures are prevented if tube drainage is employed, or if open operation is postponed until frank pus is present. It should be recalled, however, that chronic empyema is more frequent after delayed operation, and in massive synpneumonic purulent effusions and putrid empyema following the rupture of large pulmonary abscesses, it occasionally seems imperative to establish drainage before the mediastinum has become stabilized. These persons have extremely low respiratory reserve and must be guarded very carefully from even minor paradoxical respiratory movements. Likewise, immediate drainage may be necessary on the occasion of a spontaneous pyopneumothorax or so-called "tension pneumothorax" to relieve high intrathoracic pressure. Ordinarily pus is present under considerable pressure, and when thoracotomy is performed the mediastinal tissues will shift toward the affected side. The mere shift of the mediastinal structures following an ill-advised rib resection does not cause all the untoward symptoms solely because of the reduction of the respiratory reserve; they are also due to the superimposition of paradoxical respiratory movements preventing the noncollapsed portion of the lung from filling and emptying efficiently. The tidal air flows in and out of the lungs because of a difference in pressure between the air in alveolar spaces and the atmospheric air. In the absence of an adequate respiratory reserve a rather insignificant paradoxical movement might make it impossible for these differences to be established. Another abnormal mechanism which inhibits proper aeration results when air from the functioning portions of lungs is forced into the collapsed areas on expiration, and then on inspiration this same spent air flows back into the functioning portion. This phenomenon occurs when there is a considerable to-and-fro flow of air between a pleural cavity and the outside through a large hole in the chest wall.[6] The duration of the disease will not necessarily determine the mobility of the mediastinum. Where considerable pleural thickening occurs early, the mediastinal structures will become fixed in a relatively short time. In conditions such as exist in hemolytic streptococcal infections, however, fixation will not take place until much later.

Treatment with irrigations is an efficient method of removing layers of fibrin from the pleural surfaces, and as soon as these surfaces are clean, the lung will re-expand to obliterate the dead space and heal the empyema. Two conditions may prevent this course; first, rare instances of pulmonary fibrosis, and second, atelectasis due to a plugged bronchus. When re-expansion is unduly delayed, bronchoscopic examination may reveal a bronchus plugged with mucus which can be removed by direct aspiration.

It must be emphasized that consistently good results are obtained only by conscientious observation of and attention to the minute de-

tails of the treatment and course of the disease. This statement is true regardless of the form of treatment. Particular attention should be given to the patient's nutrition. Many of these patients have endured a prolonged debilitating illness and are in poor physical condition. However, when efficient drainage is established the fever disappears and the appetite is restored. A high vitamin, high caloric diet will be relished. As in most diseases affecting the respiratory apparatus, food, rest, and good hygienic conditions contribute much toward recovery.

Points in Diagnosis and Preliminary Studies.—The diagnosis of empyema frequently is overlooked because the condition is not suspected. So-called unresolved pneumonia is usually unrecognized empyema. The absence of physical signs should not be considered as sufficient to exclude the diagnosis of empyema, and x-rays should be taken. The presence of a scoliosis following pneumonia with the concavity toward the affected side is highly suggestive of empyema. The final positive diagnosis must rest on the aspiration of pus. This pus must be examined for tubercle bacilli when pyogenic organisms cannot be demonstrated. It must be realized that the pus of an empyema following pneumococcus pneumonia is frequently sterile when first obtained by thoracentesis.

At the time of making a diagnostic puncture one should be prepared to remove as much pus as possible. Pus under pressure should not be left in contact with a puncture wound. Meningitis, pericarditis, and other blood-borne infections are favored by such a procedure. Pus is removed until respiratory distress is relieved. Then air is injected and pus withdrawn alternately in small equal amounts until the cavity has been evacuated of purulent exudate. The use of a three-way cock and syringe makes this a simple bedside procedure and ensures accurate control over the quantities of fluid withdrawn and air injected.

This combined aspiration of pus and injection of air serves several functions: (1) It relieves pressure; (2) it decreases the surface area bathed by pus and so reduces toxic absorption; (3) it reduces the required frequency of aspiration in the event that thoracotomy is delayed, because the slowly absorbed air compensates for the reaccumulation of pus; (4) it keeps the cavity partly distended and lessens the likelihood of early pocket formation; (5) it permits accurate x-ray visualization of the extent and nature of the cavity; and (6) it occasionally results in a cure of the empyema.

If x-ray pictures are taken with the patient in various positions a complete and accurate outline of a cavity is obtained. A loculate cavity will show several fluid levels. Multiple cavities and cavities connected by narrow channels are easily demonstrated. An unsuspected, accompanying interlobar collection of fluid may become evident because of the visualization afforded by this double contrast technique. A knowledge of the extent and outline of the fluid collection will direct the plan of attack as well as be extremely helpful during the course of

therapy, especially should complications arise. As suggested by Danna,[4] a large quantity of air serves much better than a small amount.

While repetition of aspiration and air injection is seldom necessary before thoracotomy is done, it should be performed as frequently as necessary to relieve respiratory distress. This procedure combined with the administration of sulfanilamide will cure a certain percentage of the patients with streptococcal infections if they are not seen too late.

The Institution of Drainage.—When the decision has been made that drainage is necessary, when the pus has become thick and fibrinous, and when it has not been possible to demonstrate the presence of acid-fast organisms, simple tube thoracotomy is done. While this is ordinarily a bedside procedure, it must be done in a very exact manner. An accumulative experience has shown that certain precautions must be taken.

First, a No. 22 French urethral catheter (Robinson) of medium stiffness is selected and prepared. The size of this tube is not determined by the size or age of the patient, but by the character of the material to be removed. About one-third of the length of the catheter is cut off, and the end is cut on a bevel. Four to six small fenestras are cut in the distal two inches of the catheter. Not for the purpose of making the tube a better drain but with the idea of making its end more flexible and reducing the pressure it might exert against tissues pressed upon.

Second, the tube is placed as near the center of the cavity as possible. It is undesirable to place the tube at the edge of the cavity because healing occurs at the periphery and would encase the drainage tube in a heavy fibrous tract. Also, the tube must not come in contact with the diaphragm. Capps and Coleman[8] made an extensive study of pain arising from the human pleura by tactile stimulation of various locations. The visceral pleurae are insensitive. Stimulation of the parietal pleura causes sharp local pain due to the rich supply of sensory fibers from the intercostal nerves. The central portion of the diaphragmatic pleura receives its nerve supply from the phrenic nerve, and the peripheral rim of the diaphragmatic pleura for two to three inches is innervated by the seventh to the twelfth intercostal segments. Stimulation of the central portion of the diaphragm gives rise to pain referred to the neck through afferent impulses along the phrenic nerve and transmitted as efferent impulses out the third and fourth cervical segments. The region of maximum pain is most frequently along the ridge of the trapezius muscle and is characterized by a point of maximum pain and tenderness surrounded by a zone of hyperesthesia and hyperalgesia. Irritation of the peripheral rim of the diaphragm will cause pain referred to the lower thorax, abdomen, and lumbar region. Drainage tubes and packs against a mobile diaphragm are not tolerable. Few surgeons have escaped the embarrassing experience of operating on a child for appendicitis when the symptoms were due to an early pleurisy.

A location anterior to the posterior axillary line between the fifth and eight ribs is the site of choice for tube thoracotomy. Thus the scapula is avoided, the arm movements are not interfered with, and the patient can lie on his back without pressing on the tube.

Third, the site having been chosen, an exploratory puncture is made with a large needle, and the pressure is relieved. With the needle in place, the skin and subcutaneous tissues are incised parallel to the rib

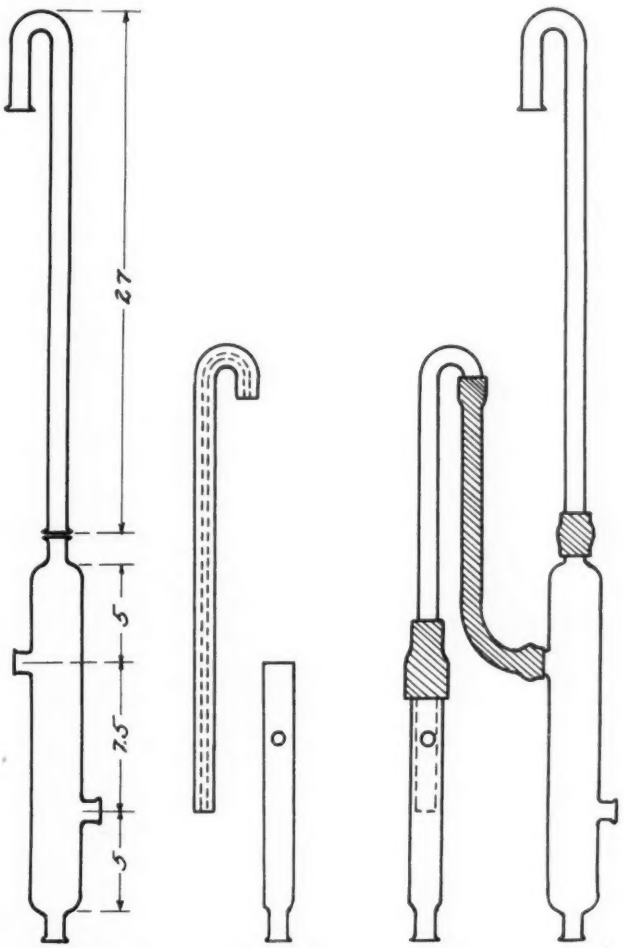

Fig. 1.—Illustrating the special glass parts of the irrigator, dimensions in centimeters and drawn to scale. The capillary siphon tube has an inside diameter of 2 mm.

Note: These dimensions should be rigidly adhered to. The "breather hole" must be present in the simple glass connector tube. (These glass parts can be obtained from Richter and Druhe, 641 Mission Street, San Francisco, Calif.)

margin. The incision must be sufficiently long to hold the tube loosely as illustrated in Fig. 4. If the skin does not fit snugly against the rubber tube, any leakage around the tube will come to the surface and will not dissect subcutaneously to form an abscess of the chest wall. In this series this complication did not occur during treatment. On

two occasions the tube was deliberately placed through pre-existing abscesses and served to drain the lesion. The course of the exploring needle being followed, a suitable trocar is passed through the chest wall into the empyema cavity. Occasionally, it is desirable to pass obliquely through the intercostal muscles. The catheter is inserted

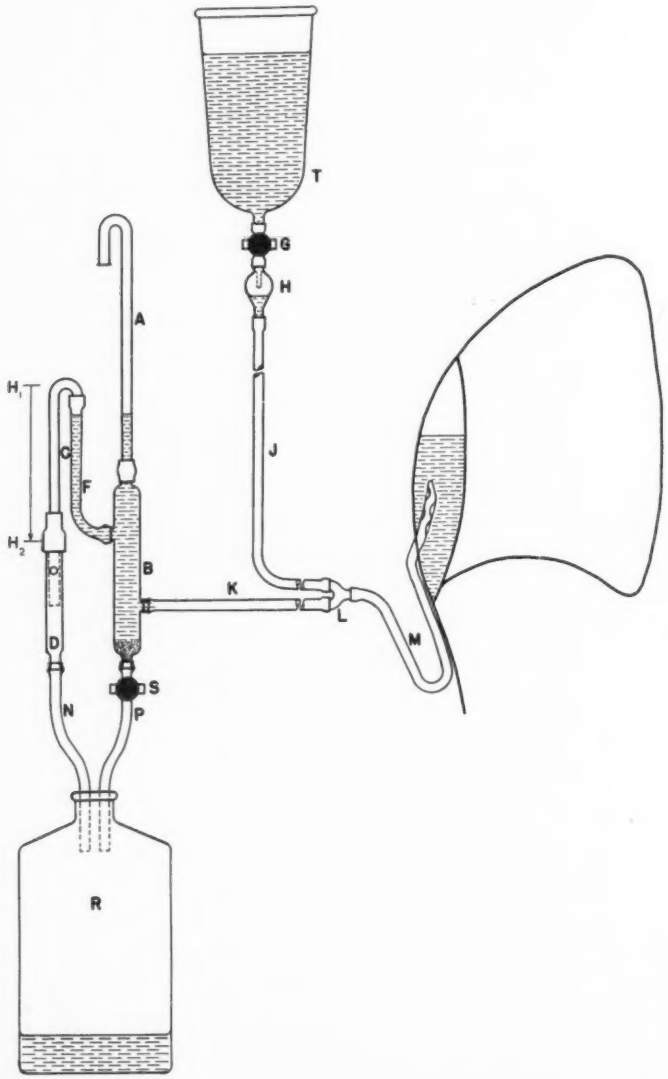

Fig. 2.—Demonstrating the assembly of the simplified irrigator and its attachment to the patient. Rubber tubes *J* and *K* should be long enough to permit the patient to sit up and turn freely. When the apparatus is attached to a small child, these tubes should be long enough to allow the child to play and to stand up in its crib. Tube *K* must not hang in a loop, because the formation of "airlocks" will interrupt free tidal irrigation.

into the cavity for a distance of three to four inches, but this is never done against resistance. The tube should extend well into the cavity for five to seven days to permit the wall of the tract to become fixed.

Should the end of the tube escape from the cavity and come to lie in the chest wall, it can seldom be replaced through the same opening. Once the tract has become stabilized by granulation tissue, the catheter is withdrawn until its lowest fenestra is about one inch inside the boundary of the parietal pleura. Externally the tube is fixed to the chest wall as shown in Fig. 4. This method of fixation contributes much to the success of the treatment and to the comfort of the patient.

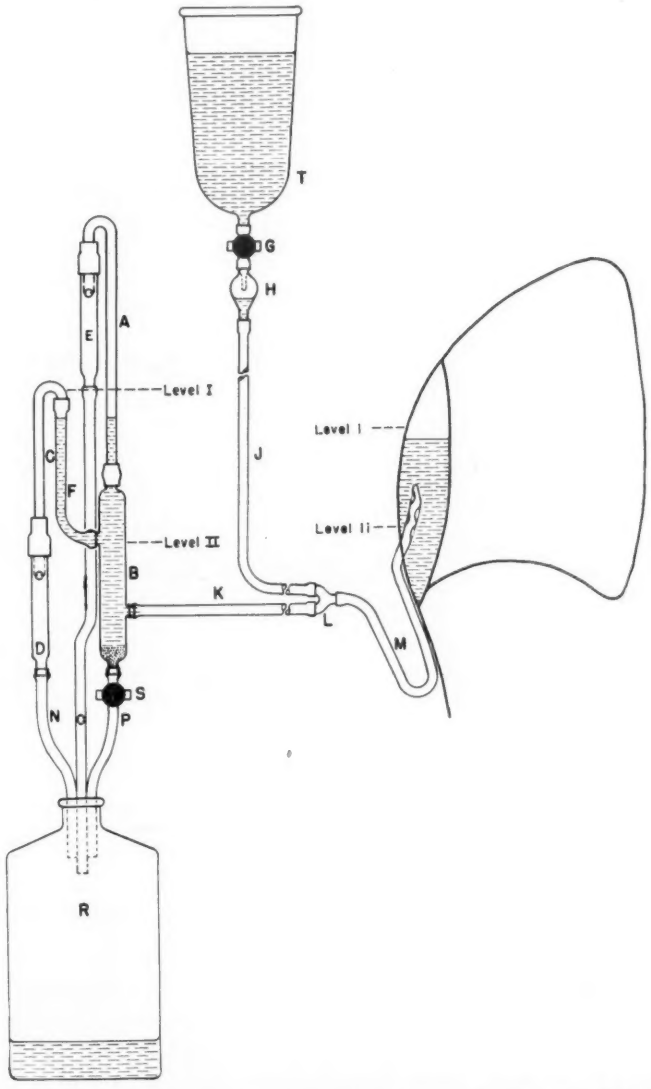

Fig. 3.—Tube *E* is added to the apparatus shown in Fig. 2. This attachment serves to carry fluid into the waste bottle *R* should the patient force fluid through *A* during a paroxysm of coughing. Stopcock *G* is adjusted to deliver 20 to 30 drops of the irrigant per minute. This fluid divides at *L* to pass into the pleural cavity or into the container *B* to change the fluid level from *Level II* to *Level I*. At *Level I* this siphon *C* overflows to drain the apparatus and the chest cavity to *Level II* and *ii* respectively.

Note: The siphon must drain slowly enough to allow emptying of the chest cavity as the fluid level in the apparatus falls. The "breather-holes" in *E* and *D* must be open.

Since the patient can move about without fear of pain from slipping and dragging of the tube, there is much less restriction of movement. Should the intercostal space be insufficient to receive the drainage tube without compression or without causing pain, a portion of rib should be resected.

The Technique of Treatment.—In the treatment of acute empyema a dynamic system is concerned, and the part cannot be placed at complete rest. Changes occur continuously which must be recognized and dealt with as soon as they take place. If the formation of a pocket is recognized early, simple distention of the general empyema cavity will break down the wall of the pocket.

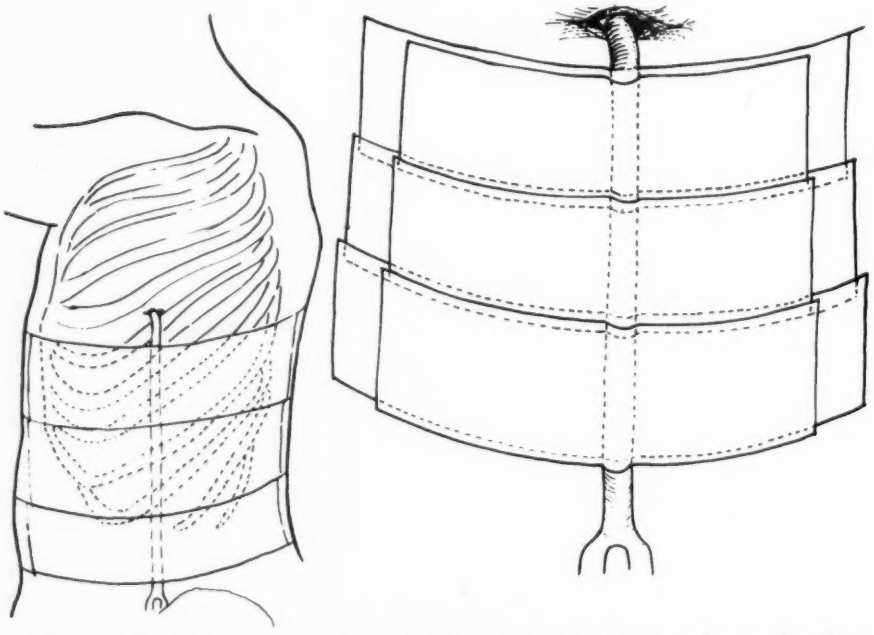

Fig. 4.—Illustrating the technique of fixing the thoracotomy tube to the chest. The skin must not fit snugly around the thoracotomy tube, which is placed in the midaxillary line whenever possible. A single sponge dressing protects the thoracotomy wound.

The irrigator (Fig. 3), filled with normal saline solution, is attached immediately after the introduction of the catheter. The top of the siphon and the outlet tube, *F*, are placed at approximately the level of the chest, *Level II*. Cock *G* is adjusted to deliver 30 to 40 drops per minute of physiologic normal salt solution continuously, which serves to wash the diluted pus out of the system beyond the catheter *M*. After twelve to twenty-four hours, depending upon the condition of the patient, the siphon tube *C* is raised to a position about 15 cm. above the outlet tube of chamber *B*. This adjustment initiates automatic tidal irrigation with a flow and ebb into and out of the cavity to dilute and wash away the exudate. Obviously, the height of the

entire apparatus determines the maximum and minimum pressures in the cavity. Continuous suction below atmospheric pressure should never be applied during the early stages of the treatment of uncomplicated acute empyema because of the likelihood of forming pockets.

The most critical period of so-called closed drainage comes within the first five days of treatment and usually during the first twenty-four hours. A "shower of fibrin" takes place due to the rather dramatic shedding of the accumulated fibrinous coat from the granulating pleural surfaces of the cavity. This material will come away in pieces much too large to pass through the drainage tube; consequently, the

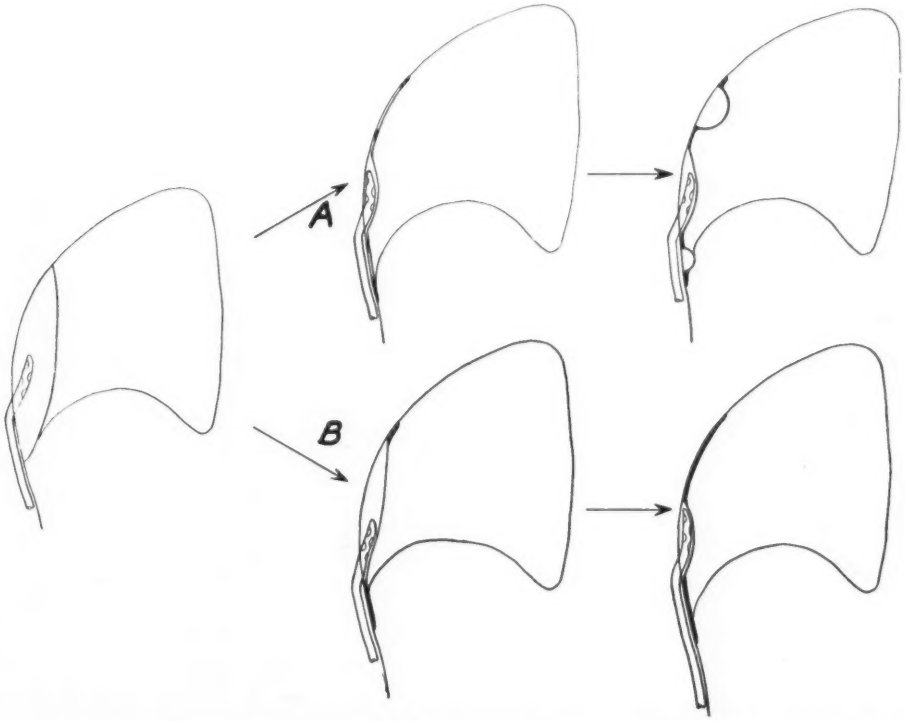

Fig. 5.—A schematic demonstration of the course of healing when: *A*, Suction is applied, the pleural surfaces are brought into contact, adhesions develop, and multiple pocket formation results; *B*, suction is not applied and healing results between the clean granulating surfaces from the periphery as the infection subsides.

tube becomes plugged. One must now patiently break up this material and slowly evacuate it. This is done by occluding tubes *J* and *K* with one hand while alternately compressing and releasing these tubes with the other hand between the point of occlusion and *L*. This procedure sets up a vigorous to-and-fro flow through the intubation catheter and will mince the particles caught in the end of the tube to a size which readily passes through the system and can be removed by washing. This operation consumes an hour or more of time, causes the patient little concern, and usually requires repetition once or twice.

Following this shower of fibrin, 500 c.c. of Dakin's solution are placed in the empty reservoir *T* twice daily. The Dakin's solution serves to dissolve and loosen fibrin and exudate if any remain; otherwise normal salt solution is used for continuous irrigation.

The use of a solution of sodium tetradecyl sulfate (1:800) and azochloramide (1:2,000) buffered to pH 7.4 as the initial irrigating agent has resulted in complete solution of the pus and the fibrinous coating of the empyema cavity in fifteen hours. The patient was a 2½-year-old Negro child with a postpneumonic empyema of three weeks' duration. The pus had the appearance of thick, split pea soup so characteristic of pneumococcal empyema. The type I pneumococcus was grown from the pus. The entire left chest was affected, with displacement of the heart and mediastinal structures completely to the right. At no time during the subsequent three weeks' period of treatment by tidal irrigation with normal saline and half-strength Dakin's solutions did pus reappear. If this experience of complete dissolution of the fibrinous deposits can be duplicated, the treatment of empyema will be greatly simplified.

The apparatus should be inspected carefully twice daily by the person in charge of the case. One will recognize at a glance, by the to-and-fro movement of fluid in the apparatus, that free communication exists between the irrigator and the cavity. After the irrigator has been emptied and washed out, the cavity is distended by pinching shut tube *K*, opening cock *G* widely, and then successively occluding and releasing tubes *J* and *K*. With tube *K* pinched shut and tube *J* open, the cavity is distended with fluid until the patient complains or coughs, until the fluid leaks out around the catheter, or until the pressure in the cavity becomes sufficient to stop the flow from the reservoir *T*. This simple procedure repeated twice daily breaks up any adhesions of unhealthy granulating surfaces and prevents pocket formation.

Leakage around the tube can be of two varieties: suction of air into the cavity and escape of fluid out of the cavity. In streptococcal infections the catheter frequently becomes loose on the fourth to the seventh day because the tissues retract and under these circumstances granulations are slow to grow out against the tube. To prevent leakage of air into the cavity the catheter is passed to fit snugly through a sheet of rubber dam which is fixed to the chest wall by adhesive ties at the four corners, or a pack impregnated with zinc oxide ointment is placed around the catheter. The outward leakage of fluid is prevented by lowering the irrigator just sufficiently to stop this flow when the apparatus is full.

In the presence of a bronchopleural fistula the irrigator, full of fluid, is lowered until coughing is no longer excited. The fistula ordinarily

heals in one or two days and the apparatus can then be raised again. Dakin's solution cannot be used in the presence of a bronchopleural fistula because it will cause coughing. This rather violent coughing is frequently the first objective sign indicating the presence of a bronchopleural fistula. In the case of infants, however, the first sign may be the vomiting of Dakin's solution which has been swallowed. If a fistula does not close spontaneously, operative procedures must be undertaken.

The volume of the cavity can be followed by measuring either the amount of fluid required to fill it or the quantity obtained when the cavity is emptied. These data, however, merely give an indication of the extent to which the lung has re-expanded but do not indicate accurately the area of involved pleura. The extent of the cavity and of the pleural thickening should be followed by weekly x-ray studies by the double contrast technique previously described.

After cultures of the fluid are negative and the exudate is scanty the irrigator may be lowered to give a so-called negative pressure in the cavity. The cavity is, however, actively distended twice daily as before. Should the patient's temperature show an evening rise, the irrigator is raised again immediately.

As the size of the cavity decreases, the catheter is shortened. When the volume of the cavity is reduced to about 30 c.c., the tidal irrigations will cease, and the apparatus is detached. Lipiodol is injected and films are taken to demonstrate the possible presence of small sinus tracts. The cavity is irrigated three times daily with Dakin's solution. The use twice weekly of a generous amount of 1 per cent silver nitrate as an irrigating solution will effect a rapid obliteration of the residual cavity and tract. The use of the silver nitrate solution is both preceded and followed by irrigation with distilled water so as to minimize the amount of silver chloride precipitated. Finally, the catheter is extruded from the healing tract, which will have become so small that the tube cannot be replaced. Following two or three days' observation the patient can be dismissed from the hospital with the tract completely healed. Should the temperature rise after removal of the tube the tract will not have healed, and a small tube can be reinserted and Dakin's irrigations continued for a few more days. If healing of the tract is unduly prolonged, it might be excised and packed. In this series such a procedure has not been necessary.

Results of Treatment.—Fifty-five consecutive cases of postpneumonic empyema were treated during a period of six years extending from 1934 to 1940 (Tables I, II, and III). No cases in which the patients were treated since 1940 are included in the discussion of end results, because after a two-year period of freedom from symptoms, with negative x-ray pictures and physical examination, recurrence is unlikely.

TABLE I

A TABULATION OF THE TYPES OF CASES OF ACUTE EMPYEMA TREATED

NO. OF CASES	CAUSTIVE ORGANISM
48	Pneumococcus*
4	Hemolytic streptococcus
2	Staphylococcus
1	Putrid (ruptured lung abscess)
Total 55	

*All types of the pneumococcus infections are grouped together since the treatment and course of the disease are essentially the same.

TABLE II

AGE DISTRIBUTION AND MORTALITY

AGE (YR.)	NO. OF CASES	DEATHS	MORTALITY (PER CENT)
Under 2	9	2*	22
2 to 10	21	0	0
11 to 20	9	0	0
21 to 30	6	0	0
31 to 40	5	0	0
41 to 50	2	0	0
51 to 60	1	0	0
Over 61	2	0	0
Total	55	2	3.64

*Both of these patients had pneumococcus infections. The cause of death is discussed in the text. One death was due to meningitis and the other to fibropurulent pericarditis.

TABLE III

COMPLICATIONS ENCOUNTERED IN 55 CONSECUTIVE CASES IN WHICH PATIENTS WERE TREATED BY TIDAL IRRIGATION

COMPLICATION	NO.
Bronchopleural fistula	8
Empyema necessitatis	2 (pneumococcal)
Pericarditis (fibrinous)	1 (fatal)
Meningitis	1 (fatal)
Diabetes	1
Otitis media	10
Lung abscess	1

Two-year follow-up studies have been obtained in fifty-four of the cases. There have been no recurrences and in no patient has a chronic empyema developed.

Two deaths occurred. One patient was 9 months of age, a 7-month, premature syphilitic infant who had fully developed signs of meningitis before thoracotomy was performed; at autopsy approximately one-third of the cerebral cortex was found to be involved. The empyema cavity was empty and free of pus. The second death was that of a Chinese infant 18 months of age. This child had signs of pericarditis before thoracotomy was performed. Death occurred suddenly two days after drainage of the chest. Postmortem examination showed the empyema cavity to be empty and free of pus. A massive fibropurulent pericarditis was present. Since both patients had a fatal disease ac-

cessory to the empyema thoracis before drainage was instituted, any treatment to cure the empyema was obviously futile.

In a consideration of the length of treatment required, the cases must be divided into two groups: (1) Those in which treatment was without terminal irrigation with silver nitrate solution, and (2) those in which treatment was with terminal silver nitrate irrigations. The number of cases are about equal in each group. Without the use of the silver nitrate irrigations, the small residual cavities around the drainage catheters healed very slowly. Nearly as much time was consumed in obliterating these small tracts as was required to secure the previous healing of the large empyema cavity. From our experience with the second group it may be stated that if silver nitrate irrigations are used as soon as the cavity has been reduced to a volume of approximately 30 c.c., the entire expected period of treatment will be three to five weeks, depending upon the extent of the original effusion.

The presence of a concurrent infection such as otitis media will prolong the period of treatment. Little healing occurs as long as an active underlying pneumonic process exists.

In this series healing has occurred regularly without the reaccumulation of pus, without the development of chronic empyema, and without permanent deformity.

DISCUSSION

In this study of fifty-five consecutive cases of acute empyema, with treatment over a period of six years, the factors of periodic variation of virulence of the causative organisms and severity of the disease tend to be eliminated. Therefore, it should be possible to take the results of this study as representative of what might be expected for any average period.

It would be incorrect to leave the impression that the good results reported in this communication were entirely due to the tidal irrigator used. The apparatus does greatly simplify the handling of an individual case of empyema; but strong emphasis must be placed on the fact that the treatment was carried out in all of its minute details by only two individuals. It is entirely possible that another form of treatment would give equally good results if conducted under the same conditions of general care and attention to details. Obviously, experience in the handling of this type of case influences the course of the disease, and this fact might become of increasing importance for the individual patient if the incidence of empyema is lessened by chemotherapy in pneumonia.

The introduction of chemotherapeutic measures employing the sulfonamides and detergents will probably result in cure in a higher percentage of cases of empyema during the early stages by simple thoracentesis. The use of these agents[9, 10] combined with the technique of

aspiration and air injection as suggested by Danna[11] and McEnery and Brennemann[12] may well reduce the number of cases of empyema requiring surgical drainage.

The replacement of pus by air is a valuable aid in completely outlining the character and extent of the cavity. The use of this double contrast x-ray technique will frequently reveal an otherwise obscure, coexisting, interlobar collection of fluid.

The early obliteration of the cavity with the aid of suction will often result in multiple pocket formation, and this sequence is probably the main factor contributing to the failure of closed drainage. Early in the treatment the apparatus should be adjusted to give, during each tidal cycle, a pressure on the fluid in the cavity alternately above and below atmospheric. This procedure, together with the daily forceful distention of the cavity, prevents multiple pocket formation and permits healing at the periphery as the pleural surfaces become healthy and the lung re-expands.

During approximately the first half of this study the period of treatment was prolonged by inability to secure prompt healing of the residual drainage tract. Subsequently, prompt healing occurred following irrigation with a solution of silver nitrate.

We do not advocate the use of any single routine treatment for empyema thoracis, because success or failure in the treatment of this condition is largely due to the attention given to the details of whatever therapeutic measures are employed.

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PERFORATION OF THE CERVICAL ESOPHAGUS WITH MEDIASTINITIS

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PERFORATION of the esophagus has been in the past, and still is, a major surgical catastrophy. Numerous reports are in the literature describing this accident. Its cause may be any object that can be swallowed. In the case reported here, a broken piece of acrylic, a plastic material forming a partial upper denture, was the offending agent. Plastic material in one form or another is gaining popularity in almost every field today. As more of this valuable material is used, one should expect to see and hear of industrial accidents resulting from its use. Unfortunately, it is not radiopaque, a fact which makes localization of the offending piece very difficult and often impossible. A report on this accident is not intended to condemn plastic dentures but more to inform those using such material of the potential danger accompanying its use. Broken plastic dentures, because of their location, may cause damage to the oral cavity or to the esophagus, as in the case of this patient. Likewise because of its thin sharp edge when broken, it may cause a severe laceration or penetration of soft tissue. The ever-present bacteria found in the oral cavity and esophagus find an excellent field in the injured tissue and immediately begin their destructive processes.

In discussing surgery of the esophagus, Sauerbruck and O'Shaughnessy[1] state that factors which have enabled progress in the surgery of the gastrointestinal tract are missing in surgery of the esophagus. The stomach and intestines are readily accessible and can be freely mobilized to permit extensive repair and resection. Repair is simplified by the vital reaction of their serous coat. Should postoperative infection take place, its spread may be limited by the localizing action of omentum and peritoneum.

The esophagus is difficult to reach. There is no superfluous length. Small lacerations are difficult to repair. There is no serous external coat and little natural tendency to localize postoperative infection. The infection may involve the pleura, mediastinum, or even the pericardium.

The esophagus is a musculomembranous canal, 23 to 26 cm. in length leading from the pharynx to the stomach. The inner or mucous coat is composed of stratified squamous epithelium resting on a loose sub-

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mucous layer. Once the epithelium is penetrated by a foreign object, it meets little resistance in the loose tissue of the submucosa. The muscular coat consists of two layers of smooth muscle, an outer longitudinal and an inner circular layer.

The distance from the upper incisor teeth to the cardiac orifice is at least 37 cm. The blood supply in the upper portion is derived from the inferior thyroid artery, in the thoracic portion from the bronchial arteries and the upper five intercostal arteries. The main blood supply for the lower portion is derived from a single branch of the aorta which divides into an ascending and descending branch. The venous return from the esophagus is by way of the inferior thyroid, azygos, and hemiazygos veins. The lymphatic drainage is by way of the deep cervical glands in the upper third, the bronchial and mediastinal glands in the middle third, and the glands along the lesser curvature of the stomach in its lower third.

The nerve supply of the esophagus is derived from the vagi and the sympathetic trunk.

The relation of the esophagus to surrounding structures is especially unfortunate in regard to spread of infection. There is no anatomic block to dependent spread of infection from perforation of any portion of the organ; in fact, the esophagus itself acts as a pathway for spread into the mediastinum. The deep cervical fascia of the neck limits external spread of infection, further encouraging drainage into looser mediastinal tissue. These facts, plus the poor tendency of the esophagus to close or limit spillage from itself following perforation, make any injury to it especially dangerous, and requires prompt action on the part of the surgeon. The most frequent portion involved in perforation is the cervical portion. This fact greatly facilitates necessary surgery because of the relative ease with which the neck and superior mediastinum can be drained. Perforation of the thoracic portion is more serious because of immediate mediastinitis and because of the much more difficult posterior approach when drainage is instituted.

CASE REPORT

The patient, C. A. K., a 25-year-old white soldier, a native of Wisconsin, was admitted to the Station Hospital, Camp Stewart, Ga., Nov. 29, 1942, at 10:00 P.M. While riding a bus six hours before admission, he had been eating hard candy and broke off a piece of the plastic portion of a partial upper denture in his mouth, swallowing it. After the denture was broken and swallowed, he felt immediate pain in his throat. He ate more candy, attempting to force the particle down. The pain increased in his throat and he was able to swallow water only with great difficulty at time of admission.

Examination of the mouth and throat revealed nothing of importance. Under fluoroscopy, without barium, nothing could be seen as the plastic material is nonopaque (Fig. 1). A swallow of barium paste was given. In the upper third of the esophagus on the left there was an area where the barium had difficulty passing (Fig. 2). Once the radiopaque fluid passed this point, it descended to the stomach with ease.

Under direct esophagoscopy, a lacerated area was seen just below the cricopharyngeal pinchcock on the left (Fig. 3). The mucosa below this point was greatly swollen and inflamed, blocking the lumen, and further instrumentation was thought inadvisable. The patient was hospitalized, and since he could swallow water, he was given 2 Gm. of sulfathiazole by mouth, crushed and suspended in water, and 1 Gm. four hours later. Temperature on admission was 99° F., pulse 70. Nine hours after admission, at 7:00 A.M., Nov. 30, 1942, the patient complained of severe pain

Fig. 1.—X-ray of plate showing that the plastic material is nonopaque.

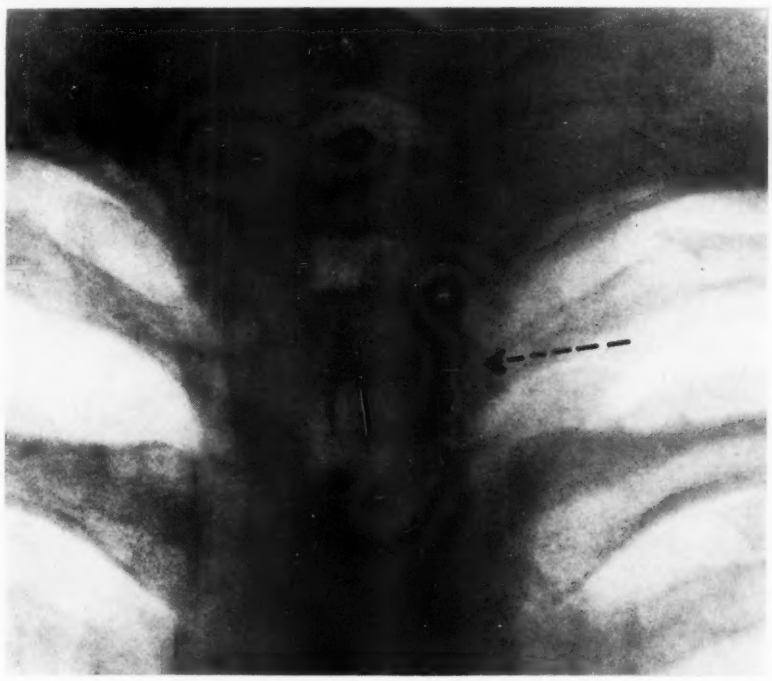

Fig. 2.—Arrow points to area in esophagus where barium collected following barium swallow.

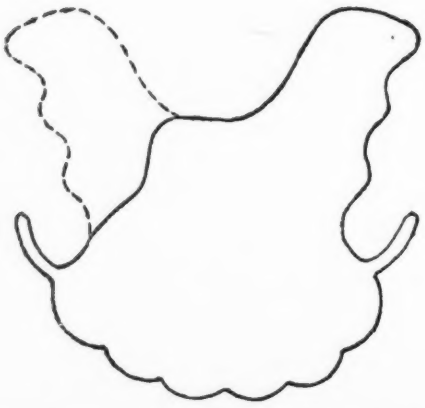

Fig. 3.—Diagram of upper denture showing broken fragment in outline.

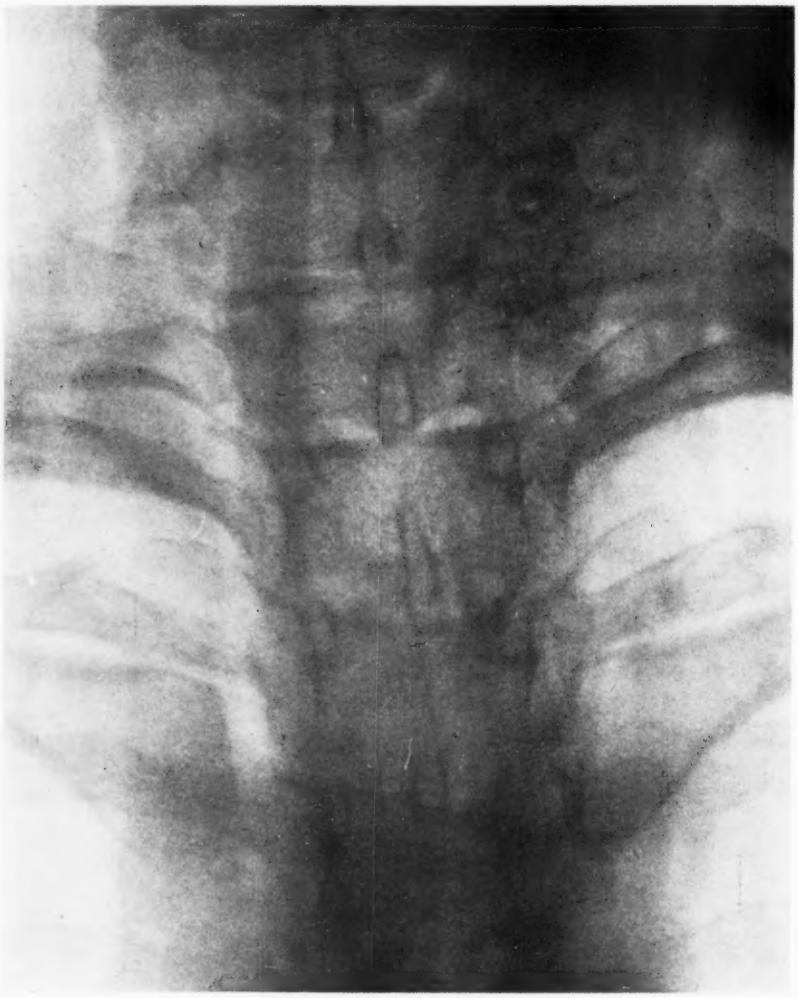

Fig. 4.—Increase in the diameter of the mediastinal shadow and air in neck prior to surgery.

in his neck and back. On paipation, there was very slight subcutaneous emphysema noted on both sides of the neck, with moderate bilateral swelling. The temperature was then 102° F. and pulse 90. All medication by mouth was discontinued and sodium sulfathiazole, 5 Gm., was given intravenously. A flat x-ray plate of the chest and neck taken at this time revealed a marked widening of the mediastinal shadow (Fig. 4). It also revealed a tissue emphysema extending from the mediastinum upward through the fascial planes of the neck. The foreign body was not visualized. One thousand cubic centimeters of 5 per cent glucose were given intravenously. At 4:00 P.M. the temperature was 103° F., pulse 120, and the patient was almost comatose. The pressure and emphysema of the neck had grown progressively worse during the day. Drainage of the neck tissues and mediastinum was decided upon and approximately twenty-four hours from the time of the accident operation was performed.

Operative Report.—Under sodium pentothal intravenous anesthesia, a six-inch incision was made along the medial border of the left sternomastoid muscle, extending within one inch of the suprasternal notch, upward. The pretracheal muscles and sternomastoid were reflected laterally from the midline and the thyroid gland exposed. The inferior thyroid vessels were ligated and the gland reflected medially. This exposed the trachea, esophagus, and carotid sheath. The carotid sheath was then followed downward close to the esophagus, by blunt finger dissection, until pulsation of the aortic arch could be easily palpated. By further blunt dissection, all muscles and fascial planes were separated, for drainage. Only a serous exudate and much air in the loose areolar tissues were encountered on the left side. On the right side of the neck the same procedure was performed and here was found frank pus within the fascial planes of the neck and around the carotid sheath, as well as serous exudate and air. Neither the injuring agent, nor the actual esophageal rent were seen at operation. Large gauze and cigarette drains were inserted into the deep spaces on both sides of the neck, packing the wound wide open, and downward into the mediastinal spaces on each side. These were anchored loosely to the skin with black silk sutures. No attempt was made to close the incisions. Time required for the operation was fifty minutes, during which 600 c.c. of 5 per cent glucose were given. Two grams of sodium pentothal were required for anesthesia, which was followed by CO_2 and O_2 inhalation when the procedure was completed. Mouth suction was used at frequent intervals during the operation. No sulfonamide preparations were applied locally.

On returning to the ward, the patient was kept in position with head low to promote drainage. Sulfathiazole, 5 Gm., was given intravenously plus 5 per cent glucose in saline solution. There was little change in the patient's condition during the night. Sixteen hours postoperative, the sulfathiazole level had reached 3.7 mg. per 100 c.c. His neck dressing was saturated with pus and serum. He was still comatose, his pulse had dropped, but his respiration and temperature continued elevated. Blood plasma was given intravenously (500 c.c.). Twenty-four hours postoperative, the temperature had risen to 104.6° F. with a rapid pulse and a lowered respiratory rate. During the day there was a marked increase in neck rigidity. His respiration had become Cheyne-Stokes in character.

In view of his surgery it was felt that the neck rigidity might be due in part to muscle spasm, but because of his generally depressed condition, meningeal irritation was suspected. A spinal puncture was done and approximately 25 c.c. of clear fluid under slight increase in pressure was removed. Thirty minutes later, 8:30 P.M., and twenty-eight hours postoperative, the patient roused from his coma for the first time and talked to the attendants. This was the first evidence of any improvement he had shown since 9:00 A.M. the previous day when he became comatose. The temperature and pulse began to decline and by the following morning his general

condition was much improved. On Dec. 2, 1942, another x-ray of the neck and chest was made (Fig. 5). This showed a decrease in the amount of air in the soft tissues of the upper chest and neck. A culture taken from the wound at the time of operation was reported: Few colonies of *Staphylococcus aureus* and *albus* (nonhemolytic), and a few colonies of streptococcus, gamma, nonhemolytic. Fluids and sulfathiazole were continued intravenously throughout the day. On Dec. 3, the patient was given one ounce of water orally with no ill effects. Since this was taken with no great difficulty, sulfathiazole was given by mouth from this time on. Dressings were changed daily, as drainage was still profuse. The drains were shortened daily.

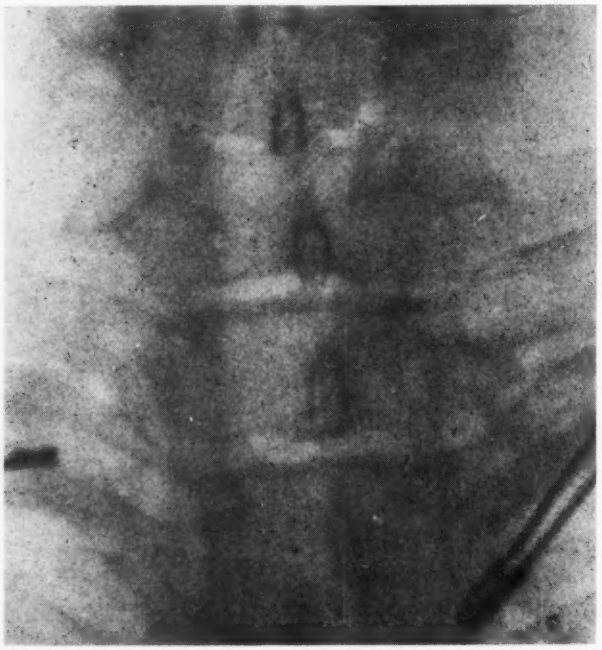

Fig. 5.—Decrease in mediastinal shadow following drainage; safety pins attached to drains in the neck.

On Dec. 4, the patient was able to take fruit juice at frequent intervals in small amounts and a supplemental intravenous injection of glucose was given to maintain his fluid level.

From this point, the progress might be considered uneventful. The fever gradually subsided and the patient regained strength. Strained soups, milk, and other nourishing liquids were added to the diet. By Dec. 9, he was given a soft diet which was well tolerated. Drainage from the wound at this time was minimal and more serous than purulent in character. On Dec. 18, the drains were removed and the wound was permitted to close (Fig. 6). The patient was encouraged to exercise in the ward. By Dec. 23, he was eating a general diet in the mess hall. On Dec. 31, he was discharged from the hospital and permission was granted for him to visit his home in Wisconsin. The broken piece of plastic which was the original offending agent was never found, though stools were searched carefully and all dressings carefully inspected. Presumably it is still somewhere in the soft tissues of the neck, or the patient unconsciously brought it up during the painful initial injury and eliminated it by mouth.

Fig. 6.—Mediastinal shadow within normal limits, twenty days postoperative.

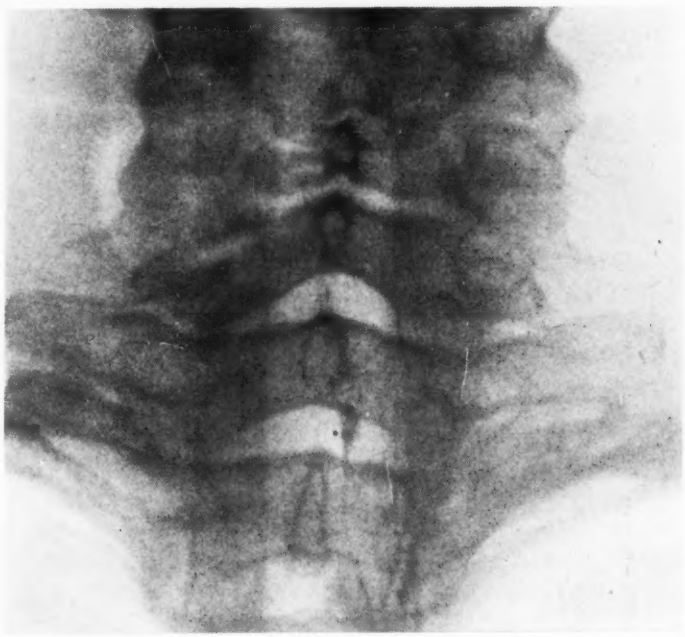

Fig. 7.—Final checkup with barium swallow; no evidence of esophageal obstruction.

On Jan. 18, 1943, following his return from leave, fluoroscopy was performed and the patient was given barium paste (Fig. 7). No evidence of any esophageal obstruction was seen. Both incision scars were well healed, pliable, and not adhered (Fig. 8). The patient was fitted with a new denture and returned to full duty.

Fig. 8.—Front view of neck showing healed scars along anterior border of sternomastoid muscles.

DISCUSSION

This case illustrates the rapidity with which infection can spread from the poorly guarded esophagus through the neck and mediastinal structures. It also illustrates the importance of early, adequate drainage of the neck and mediastinum without waiting for localization or depending upon sulfonamide therapy alone.

As recently as 1933, Pearse[2] called attention to the controversy at that time regarding choice of drainage in cases of this type, endoscopic or by external incision. More recent writers, Phillips,[3] Touroff,[4] Snyder,[5] Cummings,[6] and Carp,[7] are heartily in accord with Pearse's opinion that prompt recognition of the perforation and early external drainage will prevent many cases of mediastinitis and save many patients not improved by conservative therapy. The possible exception to this is when perforation is external, from without in, as in the case recently described by King and Straus,[8] In this type of penetration, drainage is already established and often does not need to be supplemented.

We believe that a history of swallowing a sharp object, followed by marked pain on further swallowing, and subsequent emphysema of the neck tissues are positive indications for open drainage. Sulfonamides are doubtless of value, but they should be considered only as supportive measures. Delay in the hope that infection will localize in one portion

of the neck is dangerous. We believe further that most patients will be better served by bilateral incision and drainage, even though the point of perforation can be established on one or the other side of the esophagus. The tissues surrounding the esophagus lend themselves to spread of infection across the midline as well as into the mediastinum.

In our case, earlier drainage might have prevented the appearance of the meningeal symptoms, which were unquestionably due to pressure on the great vessels of the neck by the accumulated emphysema and infection within the enveloping cervical fascia.

The operative approach to drainage of the area surrounding the esophagus and the superior mediastinal tissue was essentially that described by Pearse.[2] Drainage should be wide, as complete as possible, and maintained until all infection has cleared.

This case report and discussion are presented as a reminder that an apparently trivial accident may result in a serious surgical emergency. Temporizing or treatment with conservative means will certainly end in disaster in a large percentage of cases. Prompt, adequate, radical therapy should give a great percentage of favorable results.

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A SIMPLIFIED SUTURE-TESTING APPARATUS

CLARENCE DENNIS, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota, Minneapolis)

IN THE past few years many excellent papers have been written on the subject of suture strength and knot strength, but few of the authors have dwelt at length on the type of suture-testing apparatus used. Taylor described a device for testing knots with intermittently applied two and one-half-pound tension. Scarff described the use of a "sensitive spring scale" which was held vertically, the ends of the suture being grasped by the gloved hand, the middle looped over the hook of the scale. Schmidt-Lange fixed the ends of his strands in cellulose and strung them vertically, testing by cautious addition of weights to the lower end. Polano used a testing machine loaned by "Nähseidenfabrik Gutermann," and Howes used a "Scott thread-testing machine." The commercial machines are designed to determine not only the breaking strength, but also the elasticity of the suture or thread, and other factors. The cost of some of these commerical machines, designed for the testing of threads entering into fabrics, etc., runs in hundreds of dollars.

The conclusion one draws is that all the methods described are either inaccurate, clumsy and time-consuming, include too large a human element, or involve investment in expensive apparatus.

For the purposes of most surgeons, simple determination of the breaking strength is adequate. A simple device for this purpose is shown in Fig. 1.

The suture to be tested is wound for half a turn around each of two pulleys, the end being anchored to the first of these by a screw and to the second by two turns about a post, the loose end being held by the hand of the operator as it grasps a handle attached to this second pulley. Turning of the second pulley by means of the attached handle thus places tension on the suture to be tested, which in turn rotates the first pulley. Rotation of the latter is checked by a heavy cord attached to a coil spring in such fashion as to stretch the spring progressively with each increment in tension of the suture to be tested. A light, free rider-pointer is pushed along two parallel bars by the spring as it is stretched. With gradually increasing tension, the suture breaks; the spring snaps back to the original length, leaving the rider-pointer at the point of greatest stretch. The breaking strength then may be read directly from the pointer of the rider. Excessive snapping back of the first pulley is prevented by attachment of a rubber binder loosely to the surface of it

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in such position that no tension is placed on it except in absorbing the recoil after the breaking of the suture being tested.

For sutures of greater tensile strength, a smaller diameter pulley is mounted with the free pulley (see *inner pulley*, Fig. 1); a separate scale indicates values when this is used. The cost of the materials for this device was forty-five cents.

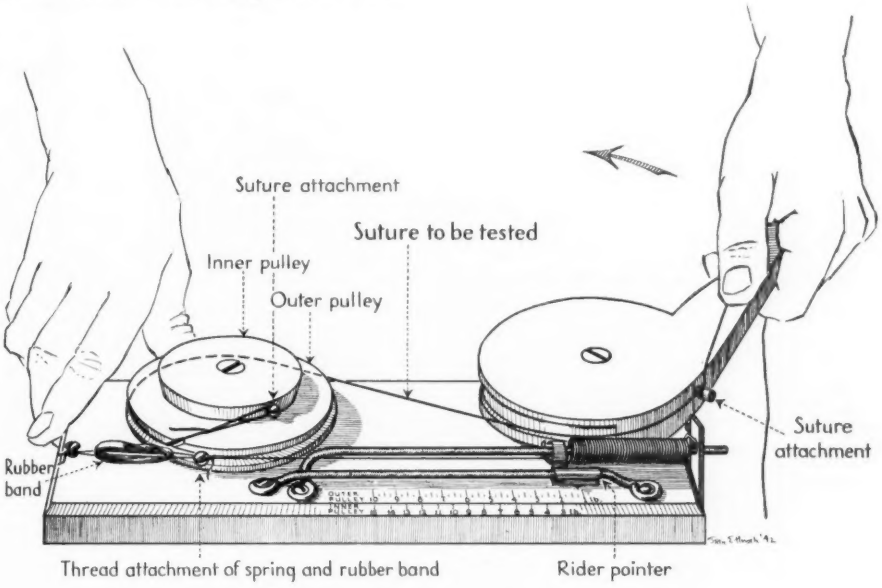

Fig. 1.—Simplified suture testing apparatus.

In practice, the suture uniformly breaks at a point not in contact with either pulley. Repeated tests on successive pieces of surgical silk from the same spool have shown results consistent within four ounces on many repeated tests.

SUMMARY

Need for a simplified suture testing device exists. Such a device is described.

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In Memoriam

MONT ROGERS REID

1889-1943

Dr. Mont Rogers Reid died May 11, 1943, at the age of 54 years, after a brief illness. His death is a great loss, not only to American surgery, but also to the community in which he lived and to his many friends and associates. Reid was a great man in the true sense of the expression, a civic leader, a great teacher, and one of the nation's great surgeons. His almost infinite interest led to achievement in many fields. The training school for surgeons which he headed was one of the best known in the country, and every year he turned out young men eager to carry out his methods. He inspired all who come in contact with him, to industry and activity, at the same time gaining their devotion by his own modesty and unselfishness. His death is a great loss to SURGERY, of which he was for years a member of the editorial board.

He was born April 7, 1889, at Oriskany, Va., the son of Benjamin Watson and Harriet Pendleton Reid. After receiving the A.B. degree at Roanoke College, he attended the Johns Hopkins Medical School, where he was graduated in 1912. He continued his surgical training at the Johns Hopkins Hospital, where he soon became known as one of the most gifted pupils of the great William Stewart Halsted.

In 1922, he came to Cincinnati as associate professor of surgery, and soon became identified with the life of the city. During 1925 to 1926 he served as visiting professor of surgery at the Peking (now Peiping) Union Medical College in China. In 1931, he was appointed professor and head of the department of surgery at the University of Cincinnati, which position he held at the time of his death.

Reid became interested in the surgery of great blood vessels while still at Hopkins, an interest which he retained throughout his career, and which led to his becoming pre-eminent in that field. In recognition of this fact, he was made the recipient of the first award of the Matas Medal in 1934. It is for his studies in the field of vascular surgery that he is best known among surgeons, but he had many other interests. His contributions to the study of the healing of wounds are well known, but in addition he wrote important articles on the surgery of the bile ducts, the thyroid gland, the sympathetic nervous system, the appendix, and many others. In recent years he was especially interested in cancer problems and as a member of the National Advisory Cancer Council had much influence on the work done in that field.

In 1942, his alma mater, Roanoke College, bestowed upon him the honorary degree, Doctor of Science. He was a member of many important surgical societies including the American Surgical Association, Southern Surgical Association, Society of Clinical Surgery, American College of Surgeons, Society of University Surgeons, Central Surgical Association, and others. In all of these he took an active part, contributing much to the value of their meetings, which he regularly attended. At the time of his death he was supervisor of research work, on

MONT ROGERS REID

the Study of Contaminated Wounds, under contract with the National Research Council, technical supervisor of the Red Cross Blood Procurement Program of Cincinnati; and director and member of the Committee of the Cincinnati Chapter of the American Red Cross. To all of these tasks, and to many others too numerous to mention, he brought the benefit of his loyalty, cool judgment, and wise counsel and advice. To those who knew him as a friend, as a teacher, or as an associate, his death has been a crippling blow and an irreplaceable loss.

—*M. M. Zinninger, M.D.*
Cincinnati, Ohio.

Book Reviews

Lymph Node Metastases. By Grantley Walder Taylor, A.B., M.D., F.A.C.S., Instructor in Surgery, Harvard Medical School; and Ira Theodore Nathanson, M.S., M.D., Instructor in Surgery, Harvard Medical School. Ed. 1. Pp. 458, with 61 illustrations and 116 tables. New York, 1942, Oxford University Press. $8.

This book is a needed addition to the sources of information for those who frequently or infrequently must make decisions regarding a plan of treatment for patients with neoplastic disease. It will be appreciated especially by the overburdened general medical practitioner who does not have the time to refer to the pathologist for knowledge of the behavior of a tumor in regard to lymph node metastasis, or to the anatomist for a description of the regional lymphatics, or to the surgical and radiological literature to complete the solution of the therapeutic problem of lymph node metastasis, not to mention the clinician and statistician for end-result studies.

The authors have achieved their purpose to assemble briefly the available information regarding the incidence of node involvement in various neoplastic diseases, the factors affecting the incidence, and the surgical management of metastases in lymph nodes.

The present volume consists of three parts. The first is a summary of the anatomy of the lymph system, and serves as a basis for the surgery of the lymphatics. Part II is a review of neoplasms of particular regions, with analysis of the incidence of node metastasis, the indication for regional dissection, and the possibility of control by surgical intervention. The role of radiation therapy of regional lymph node metastases has been briefly included, but no exhaustive effort has been made to appraise the adequacy of such treatment. Part III contains a description of standard operations, based upon orthodox procedures from the surgical literature with modifications found desirable as a result of the author's experience and studies.

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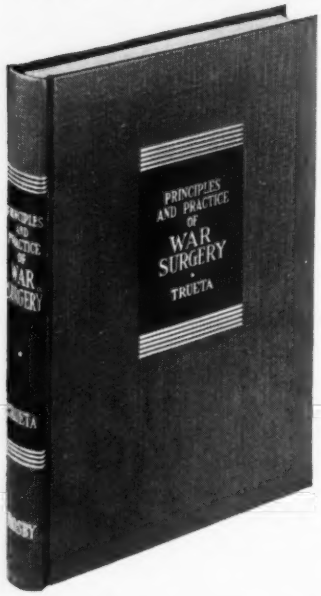

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